DISEASES OF THE CHEST

——————including the HEART

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Edited by

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Preface

No period in history has recorded the development of such effective armamentarium to prevent suffering and untimely death of the people of the world as the twenty years just past Enough has already been accomplished to assure this period the designation "The glory of Twentieth Century medicine Drugs have become available which control most bacterial and even some fungus infections of the respiratory tract Advances in bacteriology and cytology together with methods of procuring materials for such examination from within the chest have greatly improved the most important aspect of medicine namely accuracy in diagnosis For some conditions that has made prompt specific treatment possible Surgeons and their allies have unlocked many of the secrets of the chest including the heart and have developed such effective techniques as to be able to remove life time incapacitating and even early fatal conditions of the lungs bronchi and trachea They now repair cardiac abnormalities both congenital and acquired thus converting many permanent invalids to full working capacity with essentially normal life expectancy They repair injuries to the heart and great vessels which throughout all the past were fatal

The surgeon s allies include anatomists who learned that pulmonary lobes are divided into individual segments each of which can be removed as conditions warrant thus sparing normal lung tissue Recent advances in anesthesiology have made the anesthetist the surgeon s most important ally Indeed without him much present day chest surgery could not be performed Those who prepare and have ever ready an abundance of blood and plasma contribute significantly to modern chest surgery by replacing lost blood as indicated Surgical techniques have been improved and new ones devised along with special equipment such as the blood oxygenator giving the surgeon longer time for the best possible repair in open heart surgery

The chest specialist who did all diagnostic and therapeutic work alone has gone Specialties have developed within specialties so diagnosis and treatment have become a matter of teamwork Teams include internist pediatrist bronchoscopist radiologist bacteriologist pathologist anesthesiologist and surgeons Not all such persons are necessary in every case but each one must be available and called as indicated

Therefore in the preparation of manuscript for a book it is no longer possible for one physician to grasp all that is known or to write more than a small fraction of such a volume When this book was contemplated it was obvious that it could in no sense be complete without contributions of numerous persons it was also recognized that there is no substitute for experience Therefore most of the contributors have had long years of experience and actual practice and application of the subjects on which they have written To each of these authors I shall always owe a great debt of gratitude which every reader will also share They have devoted a tremendous amount of time and effort and have made many personal sacrifices in order to give the medical world what they have learned through years of study observation and hard work Each one is cognizant of the fact that nothing is final and therefore much remains to be done

Without the patience loyalty and strenuous work of Mrs Eleanor Sundstrom Mrs Kaye Swedien Miss Ruth Winter Miss Rosalind Schribman Miss Heather Claggett and Mrs Nola Pickett, this book would not have been completed

For a third of a century Charles C Thomas has devoted much time and personal attention

to considering and publishing my manuscripts He and Payne Thomas have manifested expertness in the publishing art with each volume The present book posed much time consuming hard work in the publisher s offices all of which was done carefully and cheerfully To Charles and Payne Thomas and their entire staff I again express admiration for all of their work and deep appreciation of their help and friendship through so many years

J Arthur Myers

Contents

Part II

DISEASES OF THE CARDIOVASCULAR SYSTEM

DISEASES OF THE CHEST

including the HEART

PART I

DISEASES OF THE CHEST

CHAPTER I

The Segmental Anatomy of the Lungs*

EDWARD A. BOYDEN, PH.D.

BRIEF HISTORICAL ACCOUNT

THE IMPORTANT concept embodied in the title of this chapter stems in modern times from the studies of Kramer and Glass (1932). These investigators introduced the term "bronchopulmonary segments" and provided the first diagrams of the peripheral distribution of the segmental bronchi. Strangely enough, a comprehensive monograph developing a similar point of view had been presented in 1889 by the English pathologist, William Ewart, but unfortunately it was ahead of its time and so failed to be incorporated into the literature. Thus it came about that the first clinical map of the lung, as recorded in Sauerbruch's *Chirurgie der Brustorgane* (1920), became based upon the early comparative studies of the Swiss anatomist Aeby. This pioneer investigator of the gross structure of the lungs had been convinced that the basic pattern of the bronchial tree was that of a "stem bronchus" which gave rise to alternating dorsal and ventral branches.

The reason why the concept of Kramer and Glass revolutionized the thinking of clinicians was that it provided a means of dividing the lung into smaller units than the lobes and thus permitted more accurate identification of the sites of lesions. The second step came in 1939 when Churchill and Belsey demonstrated that the bronchopulmonary segments were surgical units and could be resected, with resultant conservation of healthy tissue. Inevitably these catalyzing ideas stimulated a series of investigations dealing with the surgical anatomy of the lungs. Most comprehensive of these were the serial studies of Brock (1942–44). About the same time (1943) Jackson and Huber presented diagrams of the prevailing patterns of the segments and a terminology which, with slight modifications, is now universally employed. Finally it became necessary to portray the relations of the segmental bronchi to the corresponding blood vessels (Boyden, 1945) and to analyze the numerous variations in bronchial and vascular patterns (Boyden and colleagues, 1946–1953). Through empirical studies involving dissection and injection of hundreds of lungs, the prevailing pattern of each segment was ascertained. The key to most variations was found in the ectopic origin of the subsegmental bronchi and this was subsequently verified by embryologic studies (Wells and Boyden, 1954).

From this brief historical account it is obvious that if one wishes to comprehend the gross structure of the human lungs it is necessary to know the pattern of branching of the bronchial tree as far at least, as the subdivision of each segmental bronchus into its "a" and "b" branches (the subsegmental bronchi). Also it should be noted that each segmental bronchus has from 20 to 25 generations of non respiratory branches; that of these the first ten are cartilaginous bronchi, extending two-thirds to three-quarters of the distance to the surface of the lung, and that the remainder are bronchioles (Hayward and Reid, 1952). The role that these different elements play in pulmonary ventilation should also be considered (Churchill, 1953).

For a more detailed account of the history of the subject and an analysis of variations,

* The research upon which this chapter is based was partially supported by a grant from the Department of Health, Education and Welfare, National Institutes of Health.

CHAPTER 1

The Segmental Anatomy of the Lungs*

EDWARD A BOYDEN PH D

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the reader is referred to the authors book on the subject (1955) The present account will be confined to an elementary discussion of segments

THE STRUCTURAL COMPONENTS OF SEGMENTS

THE SEGMENTAL BRONCHI

Figure 1 is an anterior view of the right and left bronchial trees of the human lungs rotated a bit laterally to show the prevailing pattern of branching and the relation of the bronchi to further reduced the number by giving the common stem of the medial basal and anterior basal the latter's name While, perhaps a practical measure, it was confusing both from the larger standpoint of comparing right and

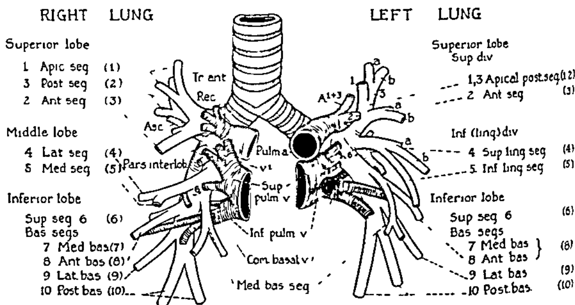


Fig 1 Diagram of anterior view of tracheo-bronchial tree with attached pulmonary arteries and veins The segmental bronchi are numbered from 1 to 10 on each side This system of numbering corresponds to that used in the authors papers on the lung from 1945 to date (The numbers in parentheses are those adopted by the International Congress of Oto-Rhino-Laryngology held in London in 1949) For explanation of other legends see text

the larger pulmonary arteries and veins at the root of the lung The segmental bronchi are numbered from 1 to 10 on each side, and are so arranged as to facilitate comparison of homologous structures The numerals in parentheses show the order of enumeration adopted by the International Congress of Oto Rhino Laryngologists held in London in 1949 (see Brock, 1950) This order is presumably based on the advantage of such enumeration to bronchoscopists and ignores other important considerations (see discussion of nomenclature in Chapter 2 of author's book) In the left lung the apical and posterior bronchi always arise together (in varying fashion) Therefore the number of segments on the left left lungs and because quite frequently the left medial basal arises separately—a circumstance which was subsequently recognized by the International Congress of Anatomists held in Paris in 1955 (see tentative list of terms adopted at that session)

THE SEGMENTAL ARTERIES

These are the branches of the pulmonary arteries which join the segmental bronchi a short distance from the hilum and thereafter distribute with the corresponding bronchi For this reason an artery can be designated by the same number as the bronchus Thus if the apical bronchus be given the symbol B^1,

ment is designated A[1] (and the corresponding vein V[1]) Frequently however an artery may arise atypically and cross intersegmental planes to reach its destination This provides one of the hazards of segmental resection

The origin and topographic relations of arteries in the two lungs are quite different On the right the pulmonary artery gives off a truncus anterior to the mediastinal side of the upper lobe then continues into the oblique fissure (as the pars interlobaris) to supply the middle and lower lobar segments Because of this relationship Aeby described the right upper lobe bronchus as being eparterial The segments of the right upper lobe which border upon the interlobar fissure are often supplied by "ascending" branches of the pars interlobaris but they may be supplied also by recurrent branches of the truncus anterior (see *Asc* and *Rec* Fig 1) Therefore in a right upper lobectomy it is necessary usually to ligate the truncus anterior and then hunt for from 1 to 3 ascending arteries at the base of the interlobar fissure Frequently these are concealed by veins (Plate 2)

In contrast the left pulmonary artery crosses the left primary bronchus wholly above the lobar bronchi Except in rare instances (Boyden 1955b) all of these bronchi are hyparterial Furthermore a left truncus anterior is infrequent Therefore in a left upper lobectomy it is necessary to follow the pulmonary artery into the interlobar fissure ligating from 4 to 7 arteries individually (Kent and Blades 1942)

THE VEINS OF THE SEGMENTS

In Figure 1 the pulmonary veins have been sketched as if they had been pulled slightly away from each bronchial tree This not only reveals their mode of branching but exposes the origin of bronchi The exact relations have been preserved in Plates 1–8 Figure 1 shows that the superior pulmonary veins drain the right upper and middle lobe and the two corresponding divisions of the left upper lobe The inferior pulmonary veins drain the lower lobes Each inferior vein arises through the confluence of a vein from the superior segment (V^6) and a vein from the basal segments the common basal vein The latter is formed by the union of superior and inferior basal veins These in turn collect the segmental veins from the basal segments

Generally speaking each segment is drained by several peripheral veins running in intersegmental or subpleural planes (and having more than one distribution) and by one deep (intersubsegmental) vein which drains the interior of the segment Since the deep one unites with one or more peripheral veins the resulting major vein can be considered a venous unit and given the same name and number as the segment from which it emerges Overholt and his associates have found this a useful concept in segmental resections so also Zenker Heberer and Lohr (1954) Cordier and Cabrol representing the opposite extreme prefer to name each vein separately Of special functional importance are the intersegmental branches of the segmental veins These will be discussed later

THE LYMPHATICS OF THE SEGMENTS

The lymphatic drainage of the segments has never been worked out as such The most recent study of drainage from the lobes is that of Nohl (1956) dealing with the spread of carcinoma in one hundred lungs removed at the time of operation

THE TOPOGRAPHIC ARRANGEMENT OF SEGMENTS

THE LOCALIZATION OF SEGMENTS IN X RAYS

A common method of teaching the relative position of segments is to employ diagrams of lungs in which the segmental bronchi have been injected with different colored masses As such diagrams are now available in most texts the writer has elected to show the position of segments as they appear when rendered opaque to the x ray Figure 2 repre

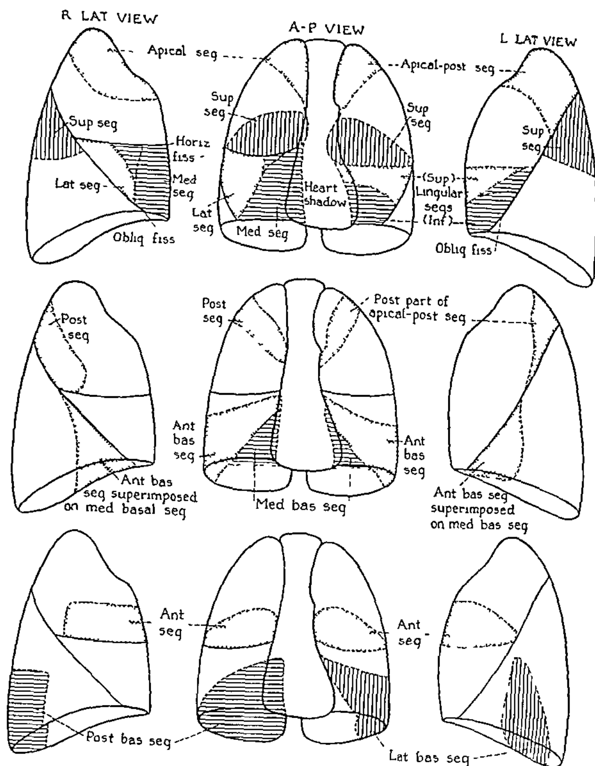


Fig 2 Diagram illustrating the location of shadows of the lung segments in roentgenograms (After Kovats, Jr and Zsebok, 1955) Note that shadows of the two segments which form the middle lobe and the lingular division of the left lung overlap each other

sents their appearance in both anterior posterior films (central column) and in lateral films (right and left columns). These figures illustrate the familiar point that one cannot identify the site of a lesion from just one film. For example in the A P view the superior segment in each lower lobe (Row 1 Fig 2) can not be distinguished from the anterior segment of the upper lobe (Row 3 Fig 2) but they are easily identified in lateral views. However it should be understood that when the parenchyma is altered pathologically as after obstructive pneumonitis the segments are frequently reduced in size or the shape of them may be otherwise distorted.

THE IDENTIFICATION OF SEGMENTAL BRONCHI IN BRONCHOGRAPHY

While it is not the purpose of this article to discuss clinical methods it may be pointed out that one of the most useful anatomical guides to the reading of bronchograms is the Wood's metal cast of the lungs depicted in Figures 126 and 127 of Brock's *Anatomy of the Bronchial Tree* (1954). For identification of subsegmental bronchi in roentgenograms see Esser (1951).

THE SEGMENTS AS THE SURGEON SEES THEM

In Plates 1 to 8 the writer has undertaken to present the lungs of a single cadaver drawn *in situ* from various exposures after the structures in the hilum have been revealed by gently sponging away the thin pleura over the roots of the great vessels and pushing back the parenchyma. Aside from preoperative aids (films bronchoscopic examination etc.) such views of the hilum provide the operator with the principal anatomical clues to the position of segments. Since these plates are made from one individual they will necessarily exhibit variations from the hypothetical norm, for no two lungs are exactly alike.

Plate 1. The mediastinal surface of the right lung. The order of structures at the hilum as one passes from superficial to deeper levels (and from lower to higher levels) is superior pulmonary vein truncus anterior of the right pulmonary artery and right upper lobe bronchus. (The latter is visible just below the azygos vein.) Enlarged lymph nodes frequently occupy the intervals between these. At still deeper levels can be seen other structures such as the pars interlobaris of the right pulmonary artery (between pulmonary vein and truncus anterior) and the artery bronchus and vein to the middle lobe. Certain intersegmental veins point to the planes which separate segments, thus the apical segment is demarcated from the anterior segment by the anterior ramus of the apical segmental vein (here labelled *Apic seg* ... the apical ramus is missing in this lung). This heads for the region just below the apical anterior notch. Similarly if superior and middle lobes are fused as is so often the case the plane of fusion is indicated by the inferior ramus of the anterior segmental vein.

Only a small area of the lower lobe is visible and this is a portion of the medial basal segment. Hidden under the right margin of the heart are the inferior vena cava the pulmonary ligament and the inferior pulmonary vein (*cf* Plate 3). This infracardiac recess may be termed the coffin corner of the right lung because here one must search for a systemic artery in the pulmonary ligament which occasionally passes from the aorta to the basal segments or even to the superior segment.

Finally note the position of the right vagus on the right lateral surface of the trachea and the relatively close approximation of the right phrenic nerve to the root of the lung. In the presence of pathological adhesions this nerve can be unwittingly injured in a lobectomy or pneumonectomy.

Plate 2. The interlobar fissures of the right lung. The right upper lobe has surfaces bordering upon both the oblique and the horizontal fissures. The two are separated by a low interfissural crest deep to which runs the posterior intersegmental ramus of the posterior vein (V^2c). The oblique surface of

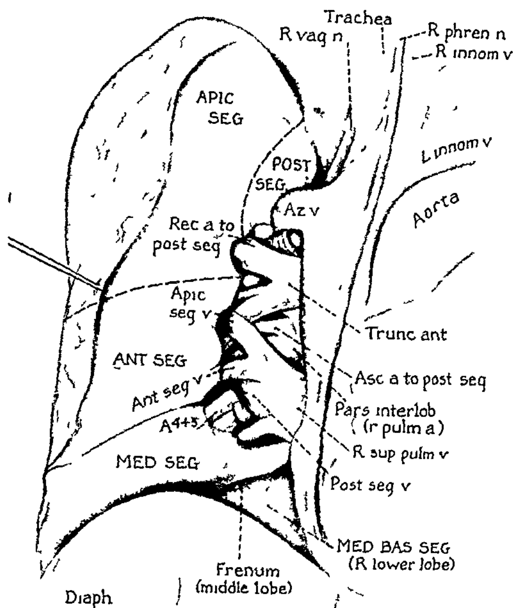


Plate I

the lobe is supplied chiefly by the posterior segmental bronchus (B^3) the two rami of which may be seen in the depths of the fissure partly covered by "ascending posterior segmental arteries (A^3) This surface of the lobe rests upon the superior segment of the lower lobe The horizontal fissural surface of the upper lobe is supplied chiefly by the posterior ramus of the anterior segmental bronchus A nearly concealed "ascending" artery (A^2a) supplies this part of the segment This surface rests upon the superior surface of the middle lobe

The middle lobe is atypical in that a supernumerary fissure separates medial from lateral segments There is one artery to the two segments which divides atypically into a branch to the lateral segment and a branch common to both lateral and medial segments In approximately half the population there are two separate middle lobe arteries and occasionally three

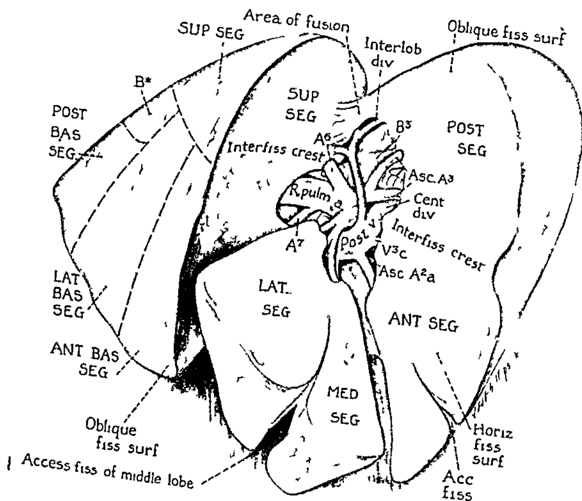


Plate 2

The fissural surface of the lower lobe is also marked by the presence of a low interfissural crest. This lies between impressions made by the upper and middle lobes. The crest marks the approximate line of separation between the superior segment and the basal segments (see also Plate 3). A^6 and A^7 indicate respectively the arteries to the superior and the medial basal segments. The segments appearing on the costal surface of the lower lobe will be discussed in connection with Plates 3 and 4.

From the surgical standpoint the relations of the vessels and bronchi in the depths of the fissure are most significant. The pattern seen in any lung depends upon the manner of development of the posterior segmental vein. In about half the cases its interlobar and central divisions are equally developed. In another fourth the interlobar division drops out, thus exposing the ascending arteries. This is referred to as the "arterial type" (of Appleton). In nearly a fifth of the cases the interlobar division takes over the drainage and becomes so large as to make it difficult to see whether or not ascending arteries are present. This is the so called "venous type." In the specimen before us the interlobar division is insignificant enough to justify the use of the term "arterial type."

Plate 3. The interlobar surface of the right lower lobe and severed pedicle of the

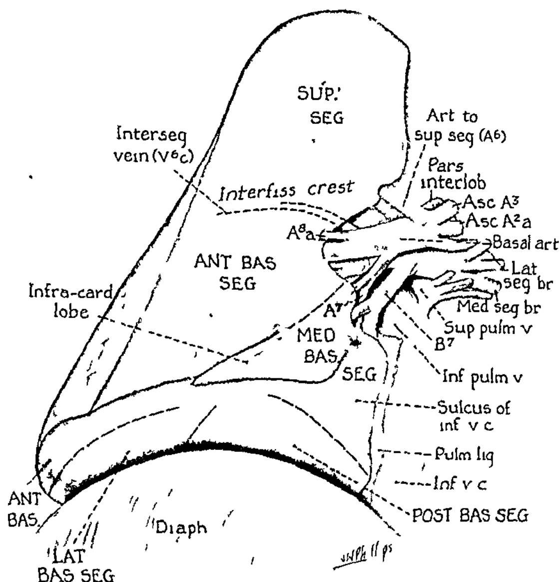


Plate 3

middle lobe *After removal of the middle lobe* certain landmarks become visible Conspicuous among these is the sulcus of the inferior vena cava Forking around this are the two rami of the medial basal bronchus (B^7) and associated artery (A^7) This bronchus is absent as such in about 20% of individuals In this specimen the presence of a supernumerary fissure converts the segment into an incomplete infracardiac lobe Such a fissure is present in over a third of individuals Normally the plane separating this segment from the anterior basal segment is demarcated by a subpleural vein the intersegmental ramus (V^8b) of the anterior basal vein Dissection along this plane affords easy anatomical approach to the basal veins and remaining basal bronchi The surface distribution of these bronchi at the base of the lung is indicated in this plate for distribution on costal surface see Plates 2 and 4

This figure also shows the branches of the interlobar portion of the right pulmonary artery—namely the ascending arteries to the upper lobe (A^3 and A^2a) the middle lobe artery, the artery to the superior segment (A^6)

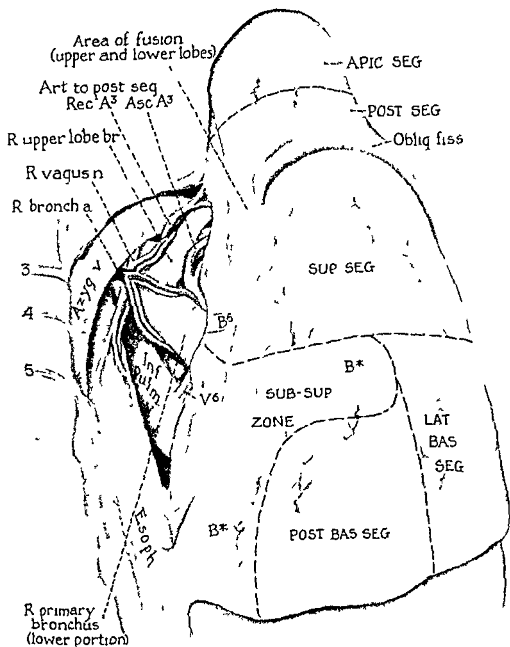


Plate 4

and the basal artery to the basal segments If this lung had been subjected to lobectomies these arteries would have been sectioned separately since they are so close together (*cf* Lindskog Liebow and Hales 1949) In 20% of cases the artery to the superior segment is represented by two or three separately originating trunks

The pedicle of the middle lobe in this specimen is drawn after having been severed, folded back towards the right and dissected into its components—namely the two segmental bronchi the single artery and the triplicate vein

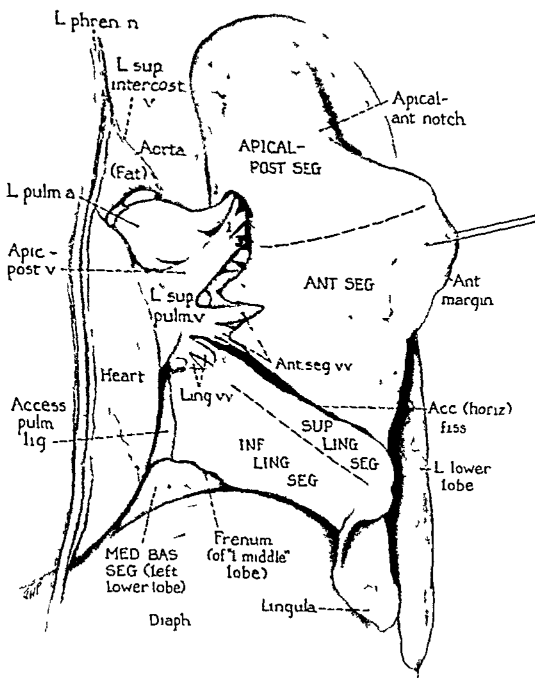


Plate 5

Plate 4 The posterior surface of the right lung In this plate the lung has been elevated but is still attached to the mediastinum The striking feature in respect to the segments is the large area occupied by the subsuperior zone indicated by the symbol B* (The asterisk is used instead of a number because of the variable site of origin of the subsuperior bronchus) In this specimen the sub superior arises on the posterior side of the lower lobe bronchus at a level between the orifices of the medial basal and anterior basal bronchi

The other feature of s interest is the right bronchial artery ay in which its bran es are tan the vagal bran e pulmo Because of t deep

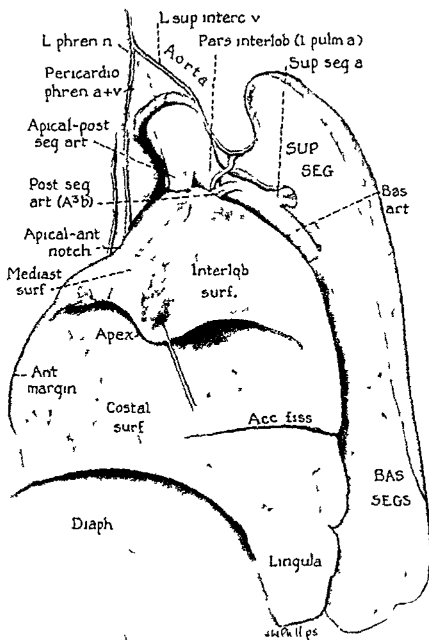


Plate 6

costal artery; hemorrhages of it are difficult to control when the artery is accidentally nicked.

Plate 5. The mediastinal surface of the left lung. The order of structures in the hilum of the left lung is different from that of the right. As one passes from superficial to deeper levels and from inferior to superior levels, the order is left superior pulmonary vein, left upper lobe bronchus and left pulmonary artery. The latter gives off arteries to the apical posterior and the anterior segment and then curves backwards and down

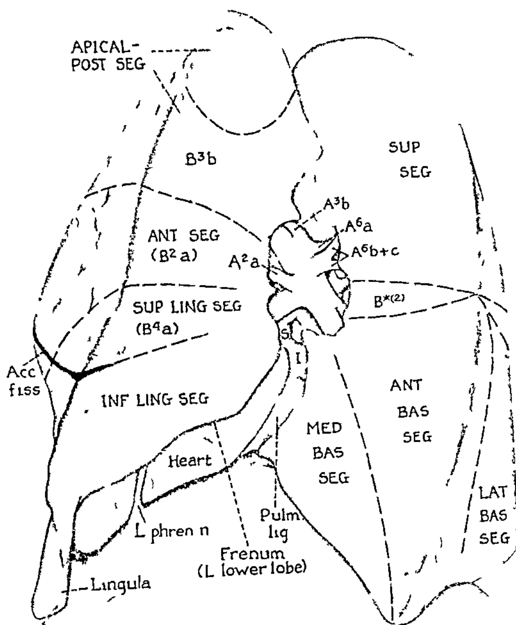


Plate 7

wards under the upper lobe bronchus to appear in the oblique fissure (see Plate 7) The vein passing over the arch of the aorta is the left superior intercostal vein better seen in Plate 8 The fat around the aorta also obscures the course of the left vagus nerve over the arch and the recurrent laryngeal branch which turns around the ligamentum arteriosum between aorta and left pulmonary artery

The superior pulmonary vein has radiating branches which point to the segments which they drain The apical vein (#1 in the figure) divides into apical and anterior rami The latter is usually intersegmental though not in this specimen Similarly the inferior ramus of the anterior segmental vein is also intersegmental separating the anterior from the superior lingular segment In this specimen it runs along the upper border of an accessory

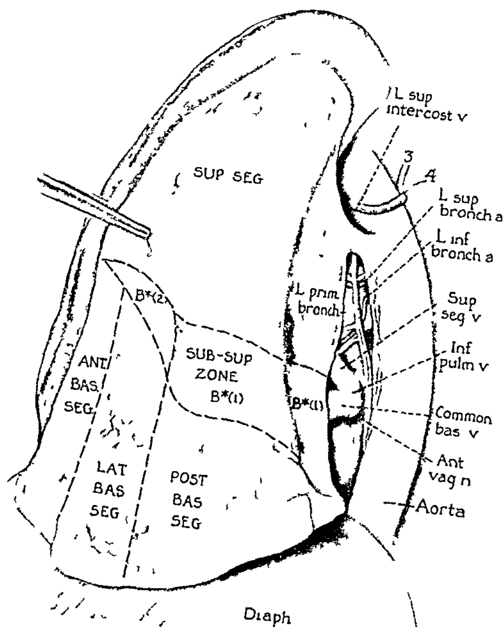


Plate 8

horizontal fissure The latter although not too deep tends to form a "left middle" lobe which is attached to the mediastinum by a separate leaflet of the pleura—an accessory pulmonary ligament The third pair of tributaries to the superior pulmonary vein are the lingular veins The upper one is intersegmental separating the superior lingular from the inferior lingular segment. The left inferior pulmonary vein is hidden beneath the pulmonary ligament

The only bronchi visible in this view are the two anterior rami of the anterior segmental bronchus Its posterior ramus (B^3a) is shown

in Plate 7. In this specimen the anterior bronchus originates from the upper lobe bronchus in the manner shown in Figure 1. But in one third of individuals *it forms the middle* member of a trifurcate upper lobe bronchus.

Only a portion of the left lower lobe is visible in this view. As on the right side, the exposed area is the medial basal segment. However, in one fourth of specimens the latter is concealed by the lower border of the upper lobe which extends downward to the diaphragm and is often congenitally fused to the medial basal segment, thereby permitting exchange of bronchi and pulmonary vessels.

Plate 6. Retracted apex of left superior lobe. The principal purpose of this drawing *is to show the position of a separate deeply* placed artery to the posterior segment (A^3b) which occurs in two fifths of specimens. This artery is shown from another aspect in Plate 7. Its occurrence may be explained by the anomalous branching of the apical posterior bronchus. As shown in Figure 1, the latter divides into apical and posterior subsegmental bronchi. However, in nearly half of the lungs the posterior ramus of the posterior division (B^3b) takes origin from the base of the apical posterior bronchus. *Therefore its artery often* arises separately and so is overlooked surgically, *with resultant hemorrhage.*

Plate 7. Surfaces of the left oblique fissure. When the superior and inferior lobes of the left lung are separated in the plane of the oblique fissure, the principal structure seen in the depths of the fissure is the pars interlobaris of the left pulmonary artery. Its branches point to the corresponding segments *on the interlobar surfaces.* Taking the upper lobe first, it will be noted that three of its four segments are represented by posterior subsegmental branches—namely B^3b, B^4a, B^5a (*cf.* Fig. 1). Curiously enough, B a is absent *in such in 35% of lungs. In such cases* adjacent bronchi take over the territory or B^2a arises from the lingular division as a displaced bronchus. Frequently the artery to this segment (A^4a) is associated with the *lingular artery.* The *intersegmental planes* between anterior and posterior and between anterior and lingular segments are occupied respectively by intersegmental branches of the posterior and anterior segmental veins (technically by V^3c and V^4c). (V^4c may be *seen on the inferior side of the lower anterior* vein in Plate 5.) Both of these are more deeply placed than the intersegmental veins of the mediastinal surface.

Turning to the interlobar surface of the lower lobe, *the most conspicuous feature is* the origin of the artery to the superior segment (A^6). It arises higher up on the pulmonary artery than the lingular artery. Therefore in a left lower lobectomy, superior and basal arteries of the lobe have to be sectioned separately; otherwise the blood supply to the upper lobe would be compromised. Also the anomalous *dual origin of arteries to the superior segment* should be noted. This occurs in a third of left lower lobes.

The superior and inferior pulmonary veins are designated by the letters S and I. As on the right side, intersegmental planes contain intersegmental veins—V^6c separating superior from basal segments, and V^8b separating anterior basal from the medial basal segment. The subsuperior zone B^* (2) will be discussed in relation to the next plate.

Plate 8. The posterior surface of the left lung. The unusual feature in this plate is the *presence* of two subsuperior zones. The first one B^* (1) is supplied by a subsuperior bronchus which arises on the posterior side of the lower lobe bronchus just opposite the orifice of the common stem of the medial basal and anterior basal bronchi. The second one B^* (2) arises one centimeter lower down from the common stem of the lateral basal and posterior basal bronchi. This is not the prevailing pattern. In three fourths of *left lower* lobes these zones would be supplied by *accessory subsuperior bronchi arising respectively* from the upper stem of the posterior basal and the lateral basal bronchus.

Turning to the posterior mediastinum one notes especially the two bronchial arteries—again accompanied by the vagal branches of the pulmonary plexus—and the left inferior pulmonary vein. As on the right side, this *venous trunk receives* a superior and a common basal vein. The latter in turn collects the veins from the basal segments of the *lung*

CONCLUDING REMARKS

To the reader who has studied these plates it must now be obvious that the anatomy of the bronchopulmonary segments is primarily a problem in topographic anatomy. Surgically, the clues to the position of segments are to be found in the hilar structures which are exposed when the thin pleura overlying the hilum is sponged off and the parenchyma pushed back. The surgeon and internist must also depend upon bronchoscopy, the usual P A and lateral roentgenograms and upon *bronchography when indicated*. Here, also striking and numerous variations tend to confuse the diagnostician. The brief survey comprised in this chapter, therefore, is only the beginning of an understanding of the subject.

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CHAPTER 2

Symptoms of Chest Diseases

Andrew I Banyai M D

Symptoms are subjective manifestations of disease which prompts the patient to seek medical attention

From the standpoint of diagnostic orientation symptoms are significant part of the over all clinical picture When properly interpreted correlated and integrated with one another their assessment may give a lead to correct exploration of the diagnostic problem

Evaluation of symptoms should always be made in the light of other pertinent data in inclusive history information on the duration of illness (possibility of congenital disease) and its relation to unusual episodes (aspiration of foreign body trauma to the chest) One should take into consideration the patient's occupation (exposure to fungi noxious fumes gases and dusts) also his habits with special reference to smoking and possible aspiration of harmful oils and lipoid material Due thought should be given to seasonal and environmental influences relative to the onset and course of the disease (inhalation of pollen and other allergens) One should keep in mind possible connection between surgical intervention x ray therapy and the patient's lung disease

COUGH

Although cough can be produced volitionally it is in its spontaneous form a reflex function of the body Its purpose is the removal of accumulated exudate mucus products of circulatory stagnation extravasated blood or foreign bodies from the respiratory tract and to rid the body from irritation of any sort which originates in the air passages Its most frequent sources are diseases of the lung the throat and the heart

Pathologic changes in any part of the respiratory system whether of infectious allergic neoplastic or other etiology may provoke cough

Extrapulmonary conditions may be associated with cough either because of secondary penetration of the lung by the pathologic process or because of pressure upon the trachea and large bronchi These include mediastinal tumors mediastinitis with or without effusion aneurysm of the large mediastinal vessels particularly the aorta double aortic arch vascular ring substernal goiter enlarged thymus enlarged hilar and mediastinal lymph nodes mediastinal emphysema inflammatory and neoplastic diseases of the pleura and the diaphragm carcinoma and diverticulum of the esophagus

Essentially cough is a variable haphazard abrupt expiratory thrust of air from the lung associated with phonation It interrupts the normal physiologic pattern of respiration Its character is influenced by the laryngeal structures competency of laryngeal innervation by the localization type and extent of the disease which provokes it the status of the respiratory muscles by the age of the patient and by the general condition of the body

Subjectively cough may be slight or severe occasional or persistent recurrent paroxysmal

loose or strenuous. Painful cough occurs in patients with pleurisy (secondary to infection, neoplasm, infarction, trauma or other causes) and following major abdominal or thoracic operations.

It is reasonable to assume that the forces of coughing are capable of evacuating inflammatory products or foreign bodies from the respiratory tract. If this is actually accomplished, one considers the cough as useful, adequate or beneficial. There are a number of instances, however, when cough is not productive of sputum or when the amount of sputum expectorated is much less than the coughing effort should have produced. This type of cough is customarily designated as unproductive or useless (tussive insufficiency).

Useless or inadequate cough may be brought about by the following circumstances:

1. The source of irritation that initiates the cough reflex is outside of the lung, as for instance in diseases of the paranasal sinuses, an elongated uvula, pressure on the trachea or bronchi by mediastinal inflammation, tumors or dilated blood vessels.

2. Noninflammatory lesions of the bronchial tubes such as benign or malignant tumors may cause persistent annoying cough without expectoration.

3. During the course of a great many inflammatory involvements of the bronchi or the lung parenchyma there is a phase when the formation of exudate is practically nil; nevertheless, the congested state of the involved structures leads to strenuous but useless cough. The best examples of this are the first stage of an acute bronchitis with a so-called dry cough and certain forms of allergic bronchitis.

4. A frequent source of inadequate cough is any disease of the lung in which the mucoid or mucopurulent products of inflammation are so tenacious, sticky and adherent to the walls of the respiratory passages that even intense exhaustive coughing is unable to remove them. The prototype of inadequate cough of this sort is that seen in the paroxysmal stage of whooping cough.

5. Accumulation of too much transudation in the alveoli in heart failure may elicit coughing that is insufficient for the cleansing of the lung.

6. There are cases in which retention of pulmonary exudates is taking place because their removal is blocked by pathological structural changes such as the formation of bronchial strictures. Such a condition often causes strenuous but ineffective coughing.

7. Atelectasis may be the source of useless cough for the reason that when the lung becomes airless distal to inflammed areas, there is no chance for the inspired air to get behind the inflammatory products that accumulate in the corresponding bronchial tubes; therefore it cannot be compressed and act as the normal expulsive force of coughing.

8. Useless cough is common in pseudohypertrophic emphysema.

Tussive insufficiency and tussive failure, regardless of their origin, are always a liability because of the stress and strain associated with coughing and also because of immediate untoward consequences.

The following table represents a list of the most important harmful sequelae of inadequate cough (tussive insufficiency and tussive failure):

(1) Interference with the healing of inflammatory diseases of the bronchi and lung parenchyma
(2) Interference with the patient's rest
(3) Rise in temperature
(4) Dyspnea
(5) Exhaustion
(6) Headache
(7) Subconjunctival hemorrhage
(8) Insomnia
(9) Loss of appetite
(10) Vomiting
(11) Urinary incontinence
(12) Postoperative disruption of wounds of the anterior abdominal wall
(13) Pain in the chest
(14) Fracture of ribs
(15) Possible droplet spread of infection from one part of the lung to another or from a lung to the opposite side
(16) Pulmonary hemorrhage
(17) Bronchiectasis
(18) Bronchospasm

(19) Lowering of the threshold of cough irritability

(20) Mediastinal emphysema (*Pneumo*mediastinum)

(21) Spontaneous pneumothorax

(22) *Subcutaneous emphysema*

(23) Cervical hernia

(24) So called hypertrophic emphysema

(25) Strain on the right ventricle of the heart

(26) Tussive syncope or its formes frustes

Trivial as it may sound it is well to point out that the intensity of cough is not always proportionate to the gravity of the provocative disease As an example one may cite instances of persistent but slight cough identified *by the patient as tickling in the* throat or as throat irritation Cough in some of these instances may be caused by primary bronchogenic carcinoma other lung tumors or mediastinal neoplasm Sensory impulses picked up by the branches of the pulmonary plexus may be transmitted to anastomosing branches of the inferior laryngeal nerve From the latter the impulses are carried to the anastomosing superior laryngeal nerve and projected to the pharynx as an irritating cough provoking sensation

In men 50 years of age or older serious consideration should be given to the possibility of carcinoma Cough is its most frequent symptom Usually it is an early manifestation Oftentimes it is remarked by the *patient that the pattern of his "cigarette* cough" has changed to the worse Cough in bronchogenic carcinoma is very difficult to control by standard doses of cough sedatives Bronchial occlusion by the tumor is likely to be followed by infection The onset of cough may be sudden in case of a complicating lung abscess It is well to keep in mind that metastatic lung tumors may cause cough while the primary neoplasm remains symptomless

Some patients say that their cough is more pronounced on changing from erect to supine position or when they bend over This should bring to mind bronchiectasis infected congenital or acquired cysts lung abscess dermoid tumor echinococcus cyst and bronchopleural fistula Also one should remember cough induced by spilling over of stagnating food particles or exudate from the esophagus in cases of cardiospasm or diverticulum of *the esophagus*

In instances when cough is more pronounced at night the following possibilities should be checked (1) failure of the right ventricle of the heart in these patients edema of the lower extremities decreases when they go to bed at the same time the lung becomes water logged" (2) benign and malignant tumors of the lung and mediastinum (3) enlargement of mediastinal lymph nodes (4) allergic bronchitis (5) bronchial asthma (6) cardiospasm (7) diverticulum of the esophagus (8) diaphragmatic hernia

Paroxysmal fits *of cough may be observed in pulmonary edema asthmatic bronchitis* bronchial asthma severe bronchitis after aspiration of foreign bodies or in connection with migration of broncholiths Also this type of cough may be associated with perforation into a bronchus of an infected lung cyst empyema mediastinal or subdiaphragmatic abscess

Early morning cough on arising may be due to cold allergy paranasal sinus infection pseudohypertrophic emphysema or bronchiectasis

Cough on swallowing may be seen in persons with developmental anomalies in the oropharynx or with esophagotracheal esophagobronchial fistulas moreover in instances where there is a sensory or motor dysfunction of the laryngeal nerves

Increase in cough after meals is a common occurrence in chronic lung diseases It is *attributable to stimulation* of the gastric nerve endings of the vagus which through a reflex arc stimulates the mucosal glands of *the bronchi In the newborn onset* of cough when it tries to nurse suggests esophageal atresia

Premenstrual congestion in the lung may be the cause of cyclically recurrent episodes of cough in young *women*

In children recurrent *episodes of cough* should be investigated among other diagnoses for allergy bronchiectasis tuberculosis congenital cystic disease lipoid pneumonia fibrocystic disease of the pancreas (mucoviscidosis) and aspirated foreign bodies Some

times strenuous exercise is followed by cough in young individuals

Bronchospasm is a common though less known cause of cough In addition to allergens irritating fumes gases and dusts bronchospasm may be provoked by any bronchopulmonary infection fibrosis congestion emphysema foreign body, broncholith undue exposure to cold and last but not least by cigarette smoking According to Romagnoli and Bird in a number of cases postoperative cough is due to reflex bronchospasm caused by traction on the stomach and splanchnic plexus during abdominal surgery

In senescence particular attention should *be given to the possibility of carcinoma emphysema* fibrosis heart failure infection and lipoid pneumonia

Recognition of allergic bronchitis as a possible cause of cough is of utmost importance This condition is much more common than generally realized It occurs in children as well as in adults It may be perennial or seasonal A great many instances of summer cough belong in this category

It is well to be aware of the fact that heart failure may be responsible for cough without overt evidence of fine moist rales over the basal areas of the lung Should this be the case digitalization and adequate doses of diuretics are bound to bring about more salutary benefits and prompter relief from cough than any of the well known cough sedatives Coughing in heart failure may become manifest earlier than dyspnea An enlarged left auricle in long standing mitral valve disease may exert pressure upon the left main bronchus and cause cough

Cough and basal rales were the conspicuous features in some of the patients of Dressler with a condition designated as post myocardial infarction syndrome The latter was characterized by pericarditis pleurisy with effusion and pneumonitis These patients suffered a recent myocardial infarction but evidence of congestive heart failure was absent

In cases suspected of having whooping cough—a term so expressive of the dominant manifestation of this disease—it is well to remember the following points (1) Similar cough may be occasionally encountered in catarrhal laryngotracheobronchitis asthmatic bronchitis bronchial asthma severe inflammatory lesions of the bronchi after aspiration of foreign bodies dislodged broncholiths neoplasms and laryngismus stridulus (2) Children who had recovered from pertussis may whoop when they contract afterwards an other severe infection of the lower respiratory tract (3) Many infants some children and adults never whoop during the course of pertussis

Cough may be observed in vocal cord paralysis from any cause

Foreign bodies loose scales and heavy cerumen in the external ear canal may result *in cough The reason for this is obvious when* one recalls that Arnold s nerve is a branch of the vagus it has anastomosis with a small branch of the glossopharyngeal nerve and that it supplies with sensory nerves the posterior and inferior portions of the external ear canal and the posterior portion of the ear drum

Psychogenic factors may be responsible for disquieting cough Mental and emotional distress may initiate a nervous reaction in the hypothalamus which is transmitted to the respiratory center and from here to the vagus Because of a consequent lag in function of the thyrohyoid muscle liquids or food particles are aspirated into the larynx Undue mental and emotional tension is bound to result in bronchospasm in some individuals Bronchospasm is one of the direct causes of cough The third form of psychogenic cough originates from a transposition of disturbing mental or emotional states into cough This represents an escape mechanism from a subjectively sensitive sphere into a symptom about which the patient feels free to complain without inhibition

In search for the cause of cough pertinent data gained through questioning observing and examining the patient are critically assayed On inspection one should note presence or absence of dyspnea cyanosis shape and mobility of each hemithorax and inspiratory descent of the diaphragm (protrusion of the epigastrium) It is well to look for Horner s syndrome which is likely to signify neoplastic involvement of the cervical sympa

(19) *Lowering of the threshold of cough irritability*

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thetic chain One should search for lymph node enlargement secondary to neoplastic metastasis or as a manifestation of some systemic disease, such as tuberculosis, sarcoidosis, Hodgkin's disease, leukemia and others Draining skin lesions may suggest actinomycosis, blastomycosis or tuberculosis Clubbing of the fingers, Hippocratic incurvation of the finger nails, disappearance of the lunulae from the latter and acroerythrosis may be observed in localized as well as in wide spread lung disease Hypertrophic osteoarthropathy may precede by several months the onset of pulmonary symptoms

Proper interpretation of x-ray findings (on fluoroscopic and/or roentgenographic examination including films taken in the standard, oblique and lordotic positions if so required, also, bronchograms and tomograms) is an essential part of diagnosis

Auxiliary procedures may be necessary to clarify the problem These include bronchoscopic examination, exploratory aspiration lung biopsy, biopsy of enlarged lymph nodes scalene "fat pad" biopsy and histologic examination of fistulas of the chest and obscure skin lesions Moreover, when circumstances require, one should resort to barium suspension for outlining the esophagus for morphological and functional studies as well as for ascertaining its relation to other thoracic structures Exploratory thoracotomy entails less postoperative invalidism than exploratory laparotomy

Laboratory examinations are indispensable for accurate diagnosis One should avail himself of microbiological examination of the sputum Aerobic and anerobic culture methods are used for the isolation of bacterial agents Search should be made for trophozoites of Entameba histolytica and for ova of parasites When there is reasonable suspicion of pulmonary infection and the patient is unable to produce satisfactory sputum specimens, fasting gastric contents should be secured for such an examination on three consecutive days Examination of the sputum or material aspirated through the bronchoscope for malignant cells may confirm the diagnosis of bronchogenic carcinoma Cytological examination of the sputum should be accepted as much a routine in older individuals with obscure lung disease as search for tubercle bacilli is done in patients suspected of having tuberculosis Furthermore cytological examination may reveal "heart failure cells," large number of eosinophilic leucocytes in instances of Loeffler's syndrome, bronchial asthma and allergic bronchitis Large number of oil-laden macrophages may be discovered in lipoid pneumonia

Skin tests serologic and hematologic studies are of great value in differential diagnosis

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PULMONARY HEMORRHAGE

Expectoration of blood, particularly in large amounts is an unpleasant and often an alarming event

Before applying any therapeutic measure it is mandatory to determine the site of the bleeding Hemoptysis may occur in inflammatory and neoplastic diseases of the nose, oral cavity and the upper respiratory tract Stomatitis, tonsillitis, paranasal sinusitis, trauma to or varices in the nose, at the base of the tongue, in the pharynx, larynx or trachea overexertion of the vocal cords, acute and chronic tracheitis, including *osteoplastic* tracheitis, foreign body in the trachea, tumors

Assuming one can rule out this type of

hemoptysis and exclude bleeding from peptic ulcer, esophageal varix, it is well to evaluate pulmonary hemorrhage in relation to the patient's age. Children, adolescents and young adults should be scrutinized first of all for possible bronchiectasis, mitral stenosis and tuberculosis. Persons, particularly men over 50 years of age should be studied for carcinoma of the lung and tuberculosis. Should this orientation fail, other possible sources of pulmonary hemorrhage should be explored. The following tables may serve as a guide in this respect.

DISEASES OF THE BRONCHI AND BRONCHIOLES

(1) Severe bronchitis and bronchiolitis due to infection or to inhalation of noxious fumes, gases, volatile oils or to thermal agents
(2) Bronchial ulcer
(3) Bronchial granuloma
(4) Bronchial tumors
(5) Bronchial varicosities
(6) Friable bronchial mucosa
(7) Broncholiths

LOBAR PNEUMONIA, BRONCHOPNEUMONIA AND PNEUMONITIS; LUNG ABSCESS

(1) Bacterial, viral, rickettsial, protozoan and parasitic infections
(2) Suppurative pneumonitis
(3) Non-suppurative pneumonitis
(4) Chronic indurative pneumonia; lipoid pneumonia
(5) Abscess formation due to pyogens, Entameba histolytica and other pathogens

LUNG TUMORS

(1) Primary bronchogenic carcinoma
(2) Sarcoma
(3) Teratoma
(4) Primary malignant melanoma
(5) Pulmonary adenomatosis
(6) Kaposi's hemorrhagic sarcoma
(7) Metastatic tumors
(8) Benign tumors

CONGENITAL PULMONARY MALFORMATIONS AND ANOMALIES

(1) Cystic disease of the lung
(2) Pulmonary arteriovenous fistula
(3) Hereditary hemorrhagic telangiectasia (Rendu-Weber-Osler disease)
(4) Increased capillary fragility
(5) Essential pulmonary hemosiderosis
(6) Tuberous sclerosis

BLOOD DYSCRASIAS

(1) Thrombocytopenic purpura
(2) Hemophilia
(3) Acute leukemia
(4) Polycythemia vera
(5) Chronic erythremia of high altitude
(6) Agranulocytopenia
(7) Pernicious anemia

HYPOVITAMINOSES

(1) Scurvy
(2) Vitamin K deficiency
(3) Vitamin C deficiency

MISCELLANEOUS CAUSES

(1) Perforation of tracheal, esophageal and mediastinal tumors into the lung
(2) Perforation of empyema into the lung
(3) Perforation of mediastinal abscess into the lung
(4) Perforation of subdiaphragmatic abscess into the lung
(5) Pulmonary manifestations of collagen diseases
(6) Wegener's disease (acute necrotizing pulmonary alveolitis with glomerulonephritis and polyarteritis)
(7) Vasomotor disturbances associated with chorea, epilepsy, cerebral hemorrhage, brain tumor, trauma to the neck and severe electric shock
(8) Vicarious menstruation

FOREIGN BODIES, TRAUMA

(1) Aspirated foreign bodies
(2) Contusion of the chest without penetrating wound

thetic chain One should search for lymph node enlargement secondary to neoplastic metastasis or as a manifestation of some systemic disease, such as tuberculosis, sarcoidosis, Hodgkin's disease, leukemia and others Draining skin lesions may suggest actinomycosis, blastomycosis or tuberculosis Clubbing of the fingers, Hippocratic incurvation of the finger nails, disappearance of the lunulae from the latter and acroerythrosis may be observed in localized as well as in wide spread lung disease Hypertrophic osteoarthropathy may precede by several months the onset of pulmonary symptoms

Proper interpretation of x-ray findings (on fluoroscopic and/or roentgenographic examination including films taken in the standard, oblique and lordotic positions if so required, also, bronchograms and tomograms) is an essential part of diagnosis

Auxiliary procedures may be necessary to clarify the problem These include bronchoscopic examination, exploratory aspiration lung biopsy, biopsy of enlarged lymph nodes, scalene "fat pad" biopsy and histologic examination of fistulas of the chest and obscure skin lesions Moreover, when circumstances require, one should resort to barium suspension for outlining the esophagus for morphological and functional studies as well as for ascertaining its relation to other thoracic structures Exploratory thoracotomy entails less postoperative invalidism than exploratory laparotomy

Laboratory examinations are indispensable for accurate diagnosis One should avail himself of microbiological examination of the sputum Aerobic and anerobic culture methods are used for the isolation of bacterial agents Search should be made for trophozoites of Entameba histolytica and for ova of parasites When there is reasonable suspicion of pulmonary infection and the patient is unable to produce satisfactory sputum specimens, fasting gastric contents should be secured for such an examination on three consecutive days Examination of the sputum or material aspirated through the bronchoscope for malignant cells may confirm the diagnosis of bronchogenic carcinoma Cytological examination of the sputum should be accepted as much a routine in older individuals with obscure lung disease as search for tubercle bacilli is done in patients suspected of having tuberculosis Furthermore, cytological examination may reveal "heart failure cells," large number of eosinophilic leucocytes in instances of Loeffler's syndrome, bronchial asthma and allergic bronchitis Large number of oil-laden macrophages may be discovered in lipoid pneumonia

Skin tests, serologic and hematologic studies are of great value in differential diagnosis

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hemoptysis and exclude bleeding from peptic ulcer, esophageal varix, it is well to evaluate pulmonary hemorrhage in relation to the patient's age. Children, adolescents and young adults should be scrutinized first of all for possible bronchiectasis, mitral stenosis and tuberculosis. Persons, particularly men over 50 years of age should be studied for carcinoma of the lung and tuberculosis. Should this orientation fail, other possible sources of pulmonary hemorrhage should be explored. The following tables may serve as a guide in this respect.

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FOREIGN BODIES, TRAUMA

(1) Aspirated foreign bodies
(2) Contusion of the chest without penetrating wound

(3) Blast injury of the lung

(4) Penetrating wound of the lung (stab wound gun shot wound injury caused by fractured rib migrating bone sequester exploratory needle)

CARDIOVASCULAR AND RENAL DISEASES

(1) Pulmonary infarction

(2) Myocardial failure with consequent pulmonary congestion or edema

(3) Pulmonary hypertension and malignant systemic hypertension

(4) Sclerosis of the pulmonary arteries and arterioles including Ayerza's disease

(5) Perforating aneurysm of the aorta or the pulmonary artery

(6) Uremia

(7) Eclampsia

(8) Renal dwarfism

INDUSTRIAL DUSTS

(1) *Silicosis*

(2) Asbestosis

(3) *Other types of pneumoconioses*

For completeness sake and for the purpose of elucidating some of the aforementioned data additional comments may be permissible

Lung Abscess Pulmonary hemorrhage is rarely the presenting symptom in lung abscess The amount of blood expectorated with each episode varies from streaked sputum to several ounces of blood

Bronchial Asthma and Allergic Bronchitis It is estimated that pulmonary hemorrhage occurs in about 4% of patients with bronchial asthma In both of these conditions bleeding from the lung may be brought about in two ways (1) by extreme congestion of the mucosa of the trachea and lower air passageways (2) by complicating infections which result from bronchial obstruction

Aneurysm There are instances of aneurysm of the thoracic aorta in which blood tinged sputum is seen for months Large aneurysm may lead to bronchial occlusion and consequent pulmonary infection with hemorrhage Nearly 5% of dissecting aneurysms are associated with pulmonary hemorrhage

Benign Tumors In patients with benign tumors of the lung bleeding may originate from the tumor itself or from bronchopulmonary infection secondary to occlusion to the lower air passages The hemorrhage may be profuse As a rule it is sudden in its onset and cessation Recurrent hemorrhages may be observed during a protracted period of time In some women with bronchial adenoma cyclically recurring hemorrhages are seen either directly before or during menstruation

Hemorrhagic Tracheobronchopathy This term was used by Jaros for the designation of a condition characterized by recurrent pulmonary hemorrhages It is attributed to increased mucosal fragility lessened function of the vasoconstrictive mechanism and to hypovitaminosis C Bronchoscopic examination reveals congestion star like suffusion or erosion and ulcer on the bronchial mucosa Lesions may be localized in the main bronchi or in the segmental or lobar bronchi

Bronchitis Blood streaked sputum is a common occurrence after strenuous coughing in bronchitis Expectoration of large amounts of blood is very rare Small hemorrhages however may recur with great frequency The amount of blood expectorated is unrelated to the 24 hour amount of sputum

Simple Bronchial Erosion Vinson in 1952 called attention to pulmonary hemorrhage originating from this source He states that the basic cause of bleeding is a small area of infection with formation of a simple hemorrhagic granulomatous mass The incident may follow "colds" (within a period of 10 to 14 days) or strenuous physical exertion or emotional tension

Broncholiths It is well to question the patient thoroughly about expectoration of small concretions In view of the great variety of causes which may result in pneumoliths hemorrhage caused by their penetration into a bronchus should not be a surprise In these instances the sputum may be blood tinged or one may encounter brisk massive hemorrhage

Primary Bronchogenic Carcinoma In patients with this condition it is not uncommon to hear about expectoration of small amounts

of blood with rather great frequency. Pulmonary hemorrhage is the presenting symptom only in about 2% of the cases.

Collagen Diseases. Pulmonary hemorrhage may be the sequel of acute pulmonary arteritis or it may result from segmental or subsegmental necrosis which is followed by cavity formation with superimposed infection and abscess.

Eclampsia. This condition may lead to hemostatic defects, namely, low platelet count, prolonged bleeding time and increased capillary fragility.

Emphysema. In patients with pseudohypertrophic emphysema there are three likely sources of pulmonary hemorrhage: (1) concomitant chronic bronchitis, (2) pulmonary hypertension, (3) infection of intrapulmonary bullae and subpleural blebs.

Hereditary Hemorrhagic Telangiectasia. This disease is frequently associated with expectoration of small amounts of blood-streaked sputum. Frank hemorrhage from the lung also occurs and it may have a fatal termination.

Enlarged Hilar and Mediastinal Lymph Nodes. Hemorrhage may result from secondary bronchial occlusion and infection. Also erosion of the bronchial mucosa or the development of bronchial varicosities may be the source of bleeding.

Pulmonary Infarction. Usually the amount of expectorated blood is only a few drachms in 24 hours. Massive hemorrhage is very rarely seen. The onset of bleeding from the lung varies from few hours to one to three days after the appearance of chest pain. The expectorated blood is bright red or dark red in color and may be of gelatinous consistency. It is observed in about 35% of patients with pulmonary infarction.

Vicarious Menstruation. I have seen unmistakable instances of pulmonary hemorrhage of this type during the menstrual period or directly preceding menstruation in young women. It has been observed that during the premenstrual period the prothrombine level is lowered and there are increased vascular permeability and capillary fragility. Sattler found on thoracoscopic examination that during the premenstrual period the pulmonary and pleural blood vessels are considerably congested and dilated.

Unusual Causes of Pulmonary Hemorrhage. Under this heading reference should be made to agammaglobulinemia complicated by pneumonia and consequent bronchiectasis. Schwartzman phenomenon has been recorded as source of pulmonary hemorrhage. The latter is rarely seen in pulmonary changes associated with lymphomatoid diseases, leukemia, Loeffler's syndrome and sarcoidosis. Endometriosis is a histologically benign but clinically malignant disease. Metastasis to the lung is rare but cases with pulmonary hemorrhage are on record. Periodic fever described by Reimann and epidemic hemorrhagic fever reported from the Orient may cause bleeding from the lung. Myasthenia gravis, regurgitation of food from the esophagus and its aspiration, eventration of the diaphragm and diaphragmatic hernia may induce pathologic changes in the lung with consequent hemorrhage. Bronchoscopic examination only exceptionally causes serious hemorrhage from the respiratory tract. Pulmonary hemorrhage was attributed to medication with gold salts, sulfadiazine, serpasil, chlortetracycline, oxytetracycline and isonicotinic acid hydrazide. My personal observations are contrary to these reports.

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PAIN IN THE CHEST

Pain is the most important sensory protective mechanism of the body. It is a common subjective signal of organic disease. Its type and modality are predicated upon the under-

lying causal changes and the degree of sensibility of the patient. Often it is one of the most pressing problems which requires immediate attention. The following grouping of possible sources of chest pain may serve as a guide in its etiologic identification.

INVOLVEMENT OF THE PLEURA

Infection (with or without effusion)
Infarction
Neoplasm
Silicosis and other pneumoconioses
Spontaneous pneumothorax
Hydropneumothorax
Hemopneumothorax
Chylothorax
Trauma
Bronchopleural fistula

DISEASES OF THE LUNG

Parenchymal and interstitial infection
Bronchial infection
Neoplasm
Aspirated foreign body
Migrating broncholith
Bronchospasm
Atelectasis
Congestion
Arteriovenous fistula
Interstitial emphysema
Air embolism
Pseudohypertrophic emphysema
Extravasated blood in the lung

DISEASES OF THE TRACHEA

Tracheitis due to infection, noxious fumes, gases, dusts or corrosives
Tumors
Aspirated foreign body
Tracheocele

DISEASES OF THE HEART AND LARGE BLOOD VESSELS

Coronary artery disease
Mitral stenosis
Aortic stenosis
arditis
Pericarditis
Aortitis
Aneurysm (aortic, pulmonary, innominate, subclavian)
Dissecting aneurysm
Ruptured aneurysm
Coarctation
Hypertension ⁄ systemic, pulmonary
Pulseless disease
Neurocirculatory asthenia
Abuse of nicotine and coffee

DISEASES OF THE MEDIASTINUM

Mediastinitis
Enlarged lymph nodes
Neoplasm
Substernal goiter
Cyst
Hernia
Perforation of the esophagus
Pneumomediastinum

DISEASES OF THE ESOPHAGUS

Esophagitis
Esophageal ulcer from regurgitating gastric juice
Neoplasm
Foreign body
Cyst
Rupture
Diverticulum
Stricture
Megaesophagus
Spasm

DISEASES OF THE DIAPHRAGM

Hiatus hernia
Diaphragmitis (Joannides-Hedblom syndrome)
Tumor

DISEASES OF THE CHEST WALL

Myositis
Fibrositis
Affections of interspinuous ligaments
Osteomyelitis

Periostitis
Tumors (primary and metastatic)
Fractures (rib, sternum, vertebrae)
Herniation of intervertebral disk
Spinal hypertrophic osteoarthritis
Tietze's syndrome
Slipped costal cartilage
Involvement of intercostal lymph nodes
Herpes zoster
Neuralgia
Mastitis
Trauma
Muscular imbalance
Spinal radiculitis
Xiphoid syndrome (xiphoidalgia)

ABDOMINAL DISEASES WITH PAIN REFERRED TO THE CHEST

Gall bladder disease
Gastritis
Gastric ulcer
Perigastritis
Periduodenitis
Aerophagia with gastric distention
Distention of splenic flexure of colon
Pylorus spasm
Gastric ptosis
Pancreatitis
Appendicitis
Normal pregnancy (rarely)

MISCELLANEOUS CAUSES

Hyperthyroidism
Hypothyroidism
Pernicious anemia
Severe secondary anemia
Cranial nerve tumor
Basal skull tumor
Tumor of spinal cord and nerves
Supranumerary cervical rib
Carotid sinus syndrome
Scalenus anticus syndrome
Tabes dorsalis
Epilepsy equivalent
Epidemic pleurodynia (Bornholm disease, myalgia caused by *Coxsackie virus group B*)
Lead poisoning
Hypoglycemia
Thiamine chloride deficiency
Pronounced tetany
Hyperventilation syndrome
Periodic disease
Impingement of scapula on the rib after thoracoplasty
Involvement of first intercostal nerve in fibrous tissue and periosteal bone formation *after thoracoplasty*
Male climacteric
Psychogenic

A few pointers on these items and other pertinent comments are offered. There are three theories relative to the causation of pleural pain which are most frequently quoted. The oldest of these is the idea that pain is provoked by friction of the two pleural *surfaces*. Mackenzie expressed the opinion that the pain of pleurisy was attributable to hyperalgesia and contraction of the intercostal muscles. The third theory was proposed by Bray. *He expressed the view that* the separation of the ribs during inspiration caused tension of the parietal pleura. Apropos of pleural pain, diaphragmatic pleurisy may lead to tenderness along the costal margin anteriorly and posteriorly, to epigastric pain or to intense abdominal pain, particularly in *children*. *Also tenderness may be present* where the imaginary extension of the tenth rib crosses the parasternal line, the site designated as "bouton diaphragmatique." Patients with diaphragmatic pleurisy *on the left side* may have pain on swallowing. I have reported cases of diaphragmatic pleurisy with consequent severe trigeminal neuralgia in which pain was promptly relieved by phrenemphraxis.

Pleural pain in silicosis and other types of pneumonoconiosis is brought about by the drift of dust particles toward the pleura. Lymph channels from an area of about 1½ cm thickness of the lung *directly adjacent to* the pleura (superficial lymphatic plexus) drain toward the pleura in contrast to the balance of the lung, the lymphatics of which drain centripetally to the hilar lymph nodes. There is an anastomosis between the superficial lymphatic plexus of the lung and the lymphatics of the pleura. Also pain in the chest in pneumonoconiosis may result from pleuropericardial adhesions, bronchospasm due to fibro-

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Ruptured aneurysm
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Hypertension (systemic / pulmonary)
Pulseless disease
Neurocirculatory asthenia
Abuse of nicotine and coffee.

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Enlarged lymph nodes
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sis, cor pulmonale with pulmonary hypertension, spontaneous pneumothorax and pseudohypertrophic emphysema.

During slow migration of pneumoliths the patient may have dull pain in the parasternal or interscapular region. Sudden perforation of a stone into a bronchus is accompanied by sharp tearing pain.

In pulmonary infarction pain is attributable to the involvement of the overlying pleura. In centrally located infarcts pain is absent. When the infarct is adjacent to the diaphragmatic pleura, pain sensation may be projected through the phrenic nerve to the cervical region. Usually pain is unilateral in pulmonary infarction. It may be moderate or severe, knife-like and worse on deep inspiration. It is most common on the right side. It may be accompanied or followed by mild shock, anxiety, dyspnea, cyanosis and rapid pulse.

Chest pain distinctly different from pain of cardiac origin was recorded in a large number of cases by Prinzmetal and Massumi (1955) as anterior chest wall syndrome. Pain was usually localized in the sternal area or cardiac apical region with spread throughout the anterior chest wall. It is associated with pronounced tenderness on light pressure. It is continuous and lasts from 4 to 6 weeks, rarely for several months. Spontaneous exacerbations of hours duration may occur and terminate gradually. Also exacerbation may follow flexion or posterior extension of the neck or the trunk or lateral rotation of the neck or chest. The onset of pain has no relation to food intake but it may be aggravated by emotional tension. As a rule it subsides at night. Respiratory, cardiac and systemic manifestations are absent subjectively as well as objectively. The syndrome has been observed in adults between the ages of 30 and 75 years. Its incidence is much higher in individuals with history of myocardial infarction than in persons who had no coronary disease.

Other clinicians noted occurrence of thoracic pain in patients who recovered from coronary occlusion. The pain was distinguishable from angina pectoris. The reader is referred to the reports of Wearn (1923) and Eckerson and his co-workers (1928).

In 1955 Miller and Texidor described "precordial catch" as a neglected syndrome of precordial pain. Their observations were summarized in the following points: "(1) All the patients have been of light or medium body build; they have been below the age of 35 years and there has been no particular sex incidence. (2) The pain is severe, sudden in onset, does not radiate and is regularly located near or above the cardiac apex. (3) The pain occurs at rest or during mild activity and is frequently related in onset to a slouched or bent over posture." They expressed the view that the pain most likely arose from the parietal pleura.

Pain of the pleuropericardial type with protracted or recurrent fever was observed by Dressler in patients who suffered a recent myocardial infarction. He designated this condition as post-myocardial infarction syndrome. In one half of his patients x-ray examination revealed findings suggestive of pericardial effusion and in 70% there was roentgenologic evidence of pleural effusion.

Exertional thoracic pain may be encountered in aneurysm of the descending aorta because of pressure on the spine.

Syndrome of the suspended heart was the diagnostic classification used by Evans and Lloyd Thomas in 13 patients on whom they reported in 1956. Chest pain was the salient and usual presenting symptom. It was localized on the left side below the breast. It was sharp or dull in character, sometimes accompanied by palpitation and loss of weight. It varied from momentary knife-like sensation to continuous pain which persisted for a week. The roentgenologic characteristics of this condition are best observed in the right and left oblique positions during deep inspiration: the heart and the diaphragm are widely separated. Their patients had no evidence of organic cardiovascular or lung disease.

In patients with attacks of acute dyspnea, chest pain and syncope one should consider the possibility of insidious thrombosis of large pulmonary arteries.

Cole and his collaborators pointed out that in asthmatic patients sudden chest pain with cough, slight elevation of temperature, increase in the respiratory and pulse rates may signalize the development of atelectasis.

In patients with postoperative pain in the chest, one should think of possible infarction bronchospasm atelectasis pneumonia, cholecystitis subdiaphragmatic abscess

Unilateral or bilateral pain may be localized in the anterior chest wall and interscapular area as part of "cervicobrachial pain syndrome" according to Johnson In some of these patients precordial pain is the chief complaint The cause of this condition is postural stress in the great majority of instances

Lipkin and his associates reported on a group of patients with pain and tenderness on gentle finger tip pressure of the xiphoid process In most instances the "xiphoid syndrome was concurrent with diseases of the heart, gall bladder stomach and esophagus Also they noted the occurrence of this syndrome without these diseases

Globus hystericus sometimes manifests itself as a sensation of distention under the sternum

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DYSPNEA

Dyspnea is disturbed abnormal breathing associated with the unpleasant subjective sensation of unsatisfied urgent need for air Objectively it is recognized as increased more or less strenuous or distressed respiratory effort

Involvement of the lung parenchyma or its supportive frame work by infection (bacterial viral protozoan parasitic or hitherto undiscovered origin) is a common cause of dyspnea The pathologic substrate may be found in the form of broncho-pneumonia lobar pneumonia miliary lesions lung abscess and interstitial pneumonitis There is no need for enumerating all conditions belonging in this category but mention can be made of pneumococcal tuberculous and mycotic lesions syphilis schistosomiasis echinococcosis tropical eosinophilosis amebiasis rheumatic fever sarcoidosis and mucoviscidosis (fibrocystic disease of the pancreas) Shortness of breath may result from pulmonary localization of collagen diseases (lupus erythematosus dermatomyositis polyarteritis scleroderma) disorders of the hemopoietic system such as lymphatic and myelogenous leukemia also certain metabolic disturbances such as xanthomatosis (Hand Schuller Christian disease) Beryllosis a form of pulmonary granulomatosis is as a rule associated with dyspnea On the other hand this symptom is not often seen in Loeffler's syndrome (eosinophilic migratory (fleeting) pulmonary infiltration] Essential pulmonary hemosiderosis (idiopathic brown induration of the lung Ceelen Gellerstedt disease) is a rare clinical condition observed almost exclusively in infants and children Dyspnea is one of its cardinal symptoms Perialveolar perivascular and interstitial fibrosis is its underlying cause Hamman Rich syndrome is another uncommon disease associated with dyspnea Its detailed discussion is presented in the chapter on Pulmonary Fibrosis Walford and Kaplan reported a new lung disease in 1957 It may be designated as pul

monary elastoclasia. Its characteristic histological manifestation is pronounced fragmentation, reduplication and thickening of the elastic fibers of the lung. The consequent intense fibrosis is progressive and it is associated with dyspnea, cyanosis, pulmonary hemorrhage and cor pulmonale. Duration of disease is from 1 to 21 years. Death results from cardiopulmonary failure.

Neoplasms of the lung (benign or malignant, primary or metastatic) are bound to lead to dyspnea in four ways: (1) by implicating large areas of the lung tissue; (2) by compression of substantial part of the parenchyma; (3) by occlusion of major bronchi with consequent extensive atelectasis or regional emphysema; (4) by interference with inflow and outflow of blood to and from the heart. In the latter instance it is known that in addition to this mechanical difficulty obstruction of the superior vena cava provokes reflex hyperventilation and dyspnea.

Massive atelectasis represents considerable loss of alveolar capillary surface area. The resulting dyspnea is likely to be aggravated by concomitant displacement of the heart and large blood vessels with consequent cardiocirculatory embarrassment. Respiratory acidosis may result from wide spread multiple small foci or large areas of atelectasis in the dependent (lowermost) lung of patient while occupying lateral recumbent position during surgery.

Dyspnea is a frequent manifestation of pulmonary fibrosis. The latter has adverse sequels which decrease the functional competence of the lung. These include encroachment upon and permanent loss of air spaces, decrease in or loss of pulmonary elasticity and distensibility, constriction of pulmonary vessels with consequent lowering of blood supply to the alveoli and other lung structures. In addition perivascular fibrosis increases resistance to pulmonary blood flow. This in turn with the ensuing failure of the right ventricle of the heart is followed by diminished pulmonary blood flow, decreased elimination of carbon dioxide and lessened uptake of oxygen. Pleuropulmonary adhesions hinder respiratory motions of the lung and when they are extensive are likely to cause ventilatory insufficiency.

Pseudohypertrophic emphysema is associated with various degrees of dyspnea throughout its clinical course. The natural history of this disease is outlined in details in another chapter. The discomfort and disability experienced by patients with this condition together with the ubiquitous prevalence of this disease should prompt the medical profession to the practice of appropriate preventive and therapeutic measures in this respect. It is regrettable indeed that one is obliged to point out that an incapacitating disease like pseudohypertrophic emphysema is one of the most neglected clinical entities in medical practice.

Shortness of breath is the chief complaint of patients who seek medical attention because of vanishing lung. The latter is characterized by the formation of giant air cysts within the lung. They are brought about by the combined influence of extensive parenchymal infection and occlusion of the terminal bronchioles by spasm, inflammatory exudate or both.

There are three congenital anomalies of the lung which as a rule are associated with dyspnea: (1) Hypogenesis and agenesis of one lung; (2) Congenital cystic disease of the lung; (3) Pulmonary arteriovenous fistula.

As the term implies hypogenesis and agenesis of one lung are the result of a developmental error. On the diseased side the main bronchus, pulmonary blood vessels and lung parenchyma may be entirely missing or they may be represented by corresponding rudimentary structures. There is a compensatory enlargement of the "good" lung on the opposite side. Dyspnea together with other symptoms and signs of respiratory insufficiency may be noted directly after birth. In other instances the individual is able to live a normal life without restriction of physical activities. Pronounced respiratory embarrassment may ensue when pleuropulmonary disease develops on the "good" side.

Congenital cystic disease of the lung is characterized by the presence of single or multiple air containing or fluid containing cysts occupying areas of lung parenchyma

he size of the cyst varies from that of honey comb to giant size corresponding to the entire extent of one lobe or one lung. Multiple smaller cysts may be found in segments of one lobe throughout one lung or both lungs. Larger cysts may be multilocular with fin like partitions. This condition may exist without symptoms for decades. In other instances symptoms suggestive of pulmonary disease such as cough expectoration hemorrhage may appear during childhood or adult life. Dyspnea or asthma like seizures may be present for years. Large cysts with check valve opening at their communicating bronchus which permits ingress of air into the cyst but prevents its egress may cause alarming dyspnea. Also respiratory distress may result from spontaneous pneumothorax a common complication of this disease.

In patients with arteriovenous fistula of the lung the presence or absence of shortness of breath is predicated upon the size of the lesion. Thus dyspnea may be absent or noticed only on exertion. It may be first experienced at birth or during early childhood gradually getting worse with age. Sometimes respiratory embarrassment becomes obvious after a serious bronchopulmonary infection. There are instances of paroxysmal nocturnal dyspnea. In others dyspnea may be so severe that the patient is completely incapacitated.

Progressive dyspnea is a salient feature of primary amyloidosis of the lung. This rare disease is characterized by amyloid infiltration of the alveolar walls and the pulmonary vessels. At the onset shortness of breath is observed on exertion only. Subsequently respiratory distress is complained of even while the patient is at rest.

Nonpenetrating trauma to chest may cause rupture of alveolar walls overlying pulmonary blood vessels. This permits the escape of air into the loose connective tissue of the vascular sheaths. Accumulation of air bubbles along the course of the latter implies a twofold interference with lung function as suggested by Macklin and Macklin in 1943 and 1944. (1) Impairment in pulmonary circulation is brought about by compression of the respective blood vessels by the invasion of air into the perivascular regions. (2) Inspiratory expansion and expiratory retraction of the lung is handicapped by the splinting action of air entrapped in the interstitial tissue. Dyspnea due to interstitial emphysema is worsened by the possible development of pneumomediastinum (mediastinal emphysema) and spontaneous pneumothorax. Rupture of alveoli with consequent penetration of air into the perivascular sheaths may occur without extraneous trauma. There are instances of spontaneous interstitial emphysema. The latter develops during severe cough during the course of a great many diseases in patients with constitutional inferiority of the alveoli or in cases where the structural integrity of the air sacs is impaired by an inflammatory process. It is my opinion that in patients with chronic bronchitis chronic parenchymal lung infections bronchiectasis bronchial asthma pulmonary fibrosis and emphysema who are getting along in reasonable comfort with their disease the sudden appearance of otherwise unexplainable severe dyspnea is most likely attributable to interstitial emphysema.

Diseases of the bronchi and bronchioles play an important role in the causation of shortness of breath. In severe bronchitis laryngotracheobronchitis and bronchiolitis with pronounced swelling of the mucosa and with profuse secretion of inflammatory exudate dyspnea demands immediate attention. Respiratory distress is associated with membranous tracheobronchitis which may develop from undue pressure of the cuff of the endotracheal tube 24 to 48 hours after endotracheal anesthesia.

Postoperative tussive insufficiency may be the cause of shortness of breath directly after major abdominal or thoracic surgery.

Bronchial asthma is characterized by sudden attacks of dyspnea. These may appear at any time during the day but more often during the night particularly after midnight. Dyspnea is accompanied by prolonged expiration hacking cough tightness in the chest and much wheezing. The asthmatic attack may last for minutes or hours and resolves in the expectoration of thick glary tough sputum. The most severe form of bronchial asthma is known as bronchial crisis. It appears in the form of acute respiratory embarrassment ex-

treme, constant shortness of breath, very high respiratory rate, cyanosis, pronounced distress of the patient and possible collapse. The critical situation is brought about by the combined effect of sudden bronchospasm, mucosal swelling in the bronchi and bronchioles and by occlusion of the lower air passages by plugs of thick, sticky mucus. Such episodes may occur as the culmination of slowly progressive asthma or may be exaggerated forms of recurrent recent asthmatic attacks. Status asthmaticus signifies a similar condition in which the distressing dyspnea persists and appears to be refractory to standard therapeutic methods. Recovery does not take place for from 1 to 4 days. In some instances it lasts for several weeks and it may be accompanied by fever of 3 to 4 days' duration. When dealing with patients with apparently intractable asthma, it is well to remember that the immediate cause of respiratory embarrassment may be pulmonary congestion secondary to failure of the left ventricle.

Bronchospasm of non allergic origin is a frequent source of dyspnea. Because of its wide spread occurrence and because of possible serious sequels, its importance in everyday practice cannot be overemphasized. A great variety of parenchymal, bronchial and interstitial forms of lung diseases may provoke this condition through reflex influences. Dyspnea is often overlooked as a manifestation of bronchospasm due to pulmonary congestion in heart disease. Bronchospasm is frequently the result of a reflex which may originate from extrapulmonary areas innervated by the vagus nerve or through direct or indirect transmission of nerve impulses from the pleura, mediastinum, chest wall or the diaphragm. Other important causes of bronchospasm with dyspnea are atmospheric contaminants such as smoke, smog sulfur dioxide, and other industrial chemicals, smoking and cough. Finally, mention should be made of psychogenic influences as possible causative agents in this respect. Etiologic diagnostic and therapeutic aspects of bronchospasm have been described by the author elsewhere.

Bronchostenosis is a recognized cause of dyspnea. Partial or complete occlusion of one of the main or major bronchi may be brought about by benign or malignant neoplasms, heavy fibrosis, aspirated foreign bodies, broncholiths. Also, it may result from compression by enlarged thymus, anomalous large blood vessel, substernal thyroid or tumors of these organs, moreover, from mediastinal neoplasms, enlarged mediastinal lymph nodes, subcarinal granuloma, mediastinal cyst, tumors of the esophagus, foreign body in the esophagus and enlarged left auricle of the heart. There are instances where dyspnea resulting from atelectasis is the first overt manifestation of a large aneurysm which causes bronchial occlusion. It is well to keep in mind that one may encounter dyspnea in allergic persons, especially in children whose trachea and bronchi are soft and collapsible. Some of the implicated air passages may become partially or completely obliterated during expiration.

Heart disease (congenital or acquired) is a well known cause of dyspnea. This symptom develops under the influence of a number of factors: (1) inadequate cardiac output, (2) retarded blood flow, (3) pulmonary congestion with stiffening and decreased inspiratory distensibility of the lung, (4) pulmonary congestion resulting in engorgement of the capillaries of the bronchial mucosa with consequent narrowing of the bronchial lumen, (5) impaired diffusion of oxygen through the alveolar capillary membrane, (6) pulmonary edema which fills the alveoli and obviates the ingress of air, (7) atelectasis by bronchial compression, (8) compression of the lung by large hydrothorax, (9) reflex rapid, shallow breathing secondary to pulmonary congestion.

Shortness of breath in heart failure secondary to malignant hypertension may be aggravated by hyalin membrane formation in the lung. Also, hyalin membrane pulmonary changes may contribute to dyspnea in patients with azotemia.

Dyspnea in heart disease with pulmonary congestion or edema may be observed in the form of nocturnal cardiac asthma, evening breathlessness, shortness of breath in the recumbent position and exertional dyspnea. Cardiac asthma is likely to disappear with the appearance of right ventricular failure. Pulmonary edema with dyspnea may result from

increased capillary permeability induced by hypoxia, increased intracranial pressure and encephalitis. Also dyspnea is seen from right-left shunt in patients with paroxysmal auricular tachycardia, auricular fibrillation and flutter. In survivors from myocardial infarction dyspnea may be due to ventricular tachycardia. In infants and young children with heart disease, severe respiratory infection may precipitate cardiac failure. Hypoxia resulting from heart failure with its consequent rapid shallow breathing creates a vicious circle in that this type of respiration causes more hypoxia. Also hyperventilation leads to increased elimination of carbon dioxide. Lowering carbon dioxide tension of the blood causes increased attachment of oxygen to hemoglobin, that is, a decreased oxyhemoglobin dissociation. This in turn causes added tissue hypoxia.

Typical myocardial infarction is associated with a triad of symptoms: (1) severe substernal pain, (2) dyspnea, (3) manifestations of shock.

It is well to keep in mind that there are instances of myocardial infarction in which dyspnea is the only symptom or the dominating symptom.

Although it is well known that failure of the left ventricle of the heart is the most frequent source of pulmonary edema, the latter may result from the inhalation of noxious fumes and gases. Harrison and his associates called attention to the possible development of alveolar and interstitial edema of the lung following sudden administration of relatively large amounts of fluid intravenously to patients with deficient electrolytes, extracellular fluids and blood volume. They attribute it to dilutional hyponatremic shock. Pulmonary congestion and edema in patients with renal failure are due to water and salt retention. As emphasized by De Passe and his associates, clinical symptoms and findings are accentuated by concurrent heart failure and pulmonary infections in these cases.

In some individuals when lying on the left side, large gas bubbles in the stomach or in the splenic flexure of the large bowel may cause pronounced upward displacement of the corresponding hemidiaphragm. This in turn may provoke reflex coronary artery spasm, myocardial ischemia, with consequent pain in the chest and dyspnea.

Dyspnea may originate from pulmonary vascular disease. In addition to arteriovenous fistula and polyarteritis, one should recall primary pulmonary arteriosclerosis, Ayerza's disease, and essential pulmonary hypertension.

Dyspnea is one of the earliest symptoms of pulmonary embolism. It has been shown experimentally that pulmonary embolism elicits reflex bronchospasm. When the resulting infarction is superficial, the concomitant involvement of the pleura provokes pain. This in turn is bound to interfere with normal respiratory excursions of the chest wall and thus it aggravates dyspnea. Insidiously or acutely developing shortness of breath may be one of the symptoms of thrombotic occlusion of the main pulmonary arteries.

In rare instances metastatic carcinoma in the lung may develop in the form of extensive embolic occlusion of small branches of the pulmonary artery. Roentgenogram of the chest may be entirely negative, although the patient suffers from pronounced dyspnea.

Intense irritation of the pleura (due to infection, chemical, mechanical factors or trauma) causes reflex inhibition of the respiratory motion of the diaphragm with consequent dyspnea.

Constrictive pericarditis as well as pericarditis with massive effusion and hemopericardium are associated with shortness of breath because of mechanical interference with normal function of the heart.

Pronounced hypertension from any cause with marked elevation of the blood pressure in the left ventricle is likely to be associated with pulmonary congestion because of mitral valvular failure. Coarctation of the aorta and pulseless disease belong in this category.

Recurrent brief but severe attacks of dyspnea, instances of periodic breathing and also constant hyperventilation and shortness of breath at rest and on exertion are observed in patients with obstruction of the superior vena cava. These symptoms are attributed to cerebral venous stasis by several investigators.

Pathological changes which cause collapse

of the lung, reduce its size substantially or interfere with cardio-circulatory function by dislocation of the heart and large mediastinal blood vessels are known to result in respiratory embarrassment. In this category belong spontaneous pneumothorax, pneumomediastinum, hydropneumothorax, large pleural effusions (pleurisy), heart failure, renal failure, Meigs' syndrome, rupture of esophagus, chylothorax, primary and metastatic neoplasms of the pleura), congenital cysts in the chest, tumors of the lung, mediastinum, pleura, diaphragm and chest wall, pronounced kypho scoliosis eventration and hernia of the diaphragm, diverticulum and tumors of the esophagus, large ascites, abdominal distention in hepatomegaly, pseudomembranous and other forms of enterocolitis and abdominal tumors and cysts of extreme size. Dyspnea may occur during the late period of normal pregnancy in women who have no heart disease. Possibly, in some instances of pregnancy, dyspnea may be associated with rapid gain in weight. Pronounced obesity is frequently associated with shortness of breath. In these cases there is an enhanced requirement for oxygen carbon dioxide exchange. At the same time, the excess adipose tissue hampers respiratory excursions of the diaphragm.

Lillington and his associates recently presented proof of existence of a cardiorespiratory syndrome in extremely obese persons. The syndrome is characterized by dyspnea on exertion, cyanosis, congestive heart failure, excessive drowsiness, alveolar hypoventilation, arterial hypoxia and hypercapnia, polycythemia and pulmonary hypertension. Their patients showed no underlying lung disease or a right-to left cardiovascular shunt. Reversal of symptoms and signs can be accomplished by adequate reduction in weight.

Intense pain in the chest is bound to interfere with normal respiratory motion of the thoracic structures and thus result in dyspnea. Pertinent items are listed in another section.

Trauma to the chest may be the source of dyspnea not only because of pain but also because of pneumothorax, pneumomediastinum, interstitial emphysema, hemothorax, laceration of the diaphragm, paradoxic respiratory movements of the chest in case of fracture of three or more ribs, substantial blood loss and shock.

It is well to remember that organic pathologic changes in the central nervous system may be followed by shortness of breath. In this connection mention should be made of the following conditions. Cerebral and cerebellar tumors, subdural hemorrhage, intracranial hemorrhage, encephalo meningitis, transverse myelitis due to trauma or pressure by tumor, poliomyelitis. Wilson and Dickinson emphasized that in poliomyelitis there are factors other than damage to the medullary center of respiration, deglutition and muscles of the larynx and to the anterior horn cells which control the muscles of respiration. These are (1) habituation to respiratory alkalosis, with its increased demand for pulmonary ventilation, (2) reduction in pulmonary and thoracic compliance (reduced expansibility of the lung and chest wall); (3) psychological attitude.

Increased intracranial pressure due to tumor, hemorrhage, edema or abscess may result in slow, deep respiration or Cheyne-Stokes respiration. Postencephalitic dyspnea appears in the form of irregular tachypnea with sharp expiration. Respiratory insufficiency with dyspnea on exertion or at rest was described by Hormia in patients with cerebellar ataxia. He observed this syndrome in cases following misuse of carbromal and in individuals with arteriosclerotic parkinsonism, apoplexy, subarachnoid hemorrhage and tumor of the cerebellum.

Dyspnea may be the sequel of postdiphtheritic respiratory paralysis. Miller and his collaborators reported unusual cases of progressive muscular atrophy and amyotrophic lateral sclerosis with exertional dyspnea as the primary complaint.

Dyspnea may be secondary to severe anemia, such as that resulting from blood loss (trauma, bleeding peptic ulcer, hemorrhage caused by neoplasm, ruptured aneurysm and other causes) or from primary blood dyscrasias (pernicious anemia and others).

Some patients with myxedema complain of shortness of breath on exertion. There are instances of heart disease where respiratory

difficulties appear with the development of thyrotoxicosis

In diabetes mellitus dyspnea may be observed in two forms (1) Originating from acidosis (2) Attributable to paralysis of the respiratory muscles in coma Acidosis with concomitant dyspnea may be noted in uremia due to nephritis urinary tract obstruction and other pathologic changes in this system In some patients with chronic pulmonary disease respiratory acidosis and dyspnea are provoked by a superimposed infection

In myasthenia gravis dysfunction of the respiratory muscles is the source of dyspnea As a rule the onset is insidious although in stances of rapid development also occur In infants respiratory embarrassment may simulate asthmatic attacks with noisy breathing particularly during night or it may give the impression of laryngeal stridor seen in tetany These "attacks" are likely to disappear during subsequent years In adults with myasthenia gravis transient episodes of difficult respiration appear with increasing frequency Such respiratory distress may ensue early in the disease It may be spontaneous or it is observed in association with bronchopulmonary infection in consequence of strain upon the respiratory muscles Its duration varies from a few minutes to several hours It may be noted that the patient is unable to take a deep breath Other causes of shortness of breath and choking spells are the accumulation of mucus in the throat and inability of the patient to raise inflammatory exudate from the lower air passages

Dyspnea may be a manifestation of an anaphylactic reaction In cases of this type the patient complains of tightness in the chest and choking sensation Concomitant symptoms and signs include apprehension rapid pulse cyanosis nausea vomiting diarrhea faintness circulatory collapse and loss of consciousness

Dyspnea may be the result of poisoning which disturbs the transportation of oxygen by the blood decreases the utilization of oxygen by the tissues through depression of the respiratory center or by impairment of function of the respiratory muscles Also angioneurotic edema of the mucosa of the respiratory tract may be a contributory factor

Rapid deep pauseless hyperventilation in children should bring to mind the possibility of poisoning with salicylates particularly with aspirin

During the course of tetanus grave respiratory difficulty may be observed It may be brought about in two ways (1) by obstruction of the upper airway by trismus and inadequate control of the muscles of the tongue and pharynx (2) by severe spasm of the muscles of the chest wall and abdomen

In instances of black widow spider bite (arachnidism) painful spasm of abdominal muscles sets in about one hour after the accident The pain caused by this cramp is so severe that it interferes with respiration In the beginning pain and concomitant dyspnea are intermittent then continuous Other symptoms are noticed simultaneously such as low grade fever precordial distress headache nausea vomiting and occasionally shock delirium convulsions urinary retention or incontinence This spider belongs to the genus Lactrodectus It is found in all parts of the United States and in Southern Canada

Isler and Hedinger in 1953 and Thorsen and his associates in 1954 described a syndrome associated with metastasizing carcinoid of the small intestine The syndrome is characterized by episodes of asthma like respiratory distress together with cyanosis valvular heart failure predominantly involving the right heart with pulmonary stenosis Lembeck in 1953 found 5 hydroxytryptamine in carcinoid tumors also known as Serotonin or Enteramine Heimark and Parkin attributed the asthma like symptoms (bronchospasm and dyspnea) to sudden release of large amounts of this compound from the carcinoid Sjoerdsma and Udinfriend ascertained that in a typical case of this sort the patient's blood contained 4 0 micrograms of Serotonin per cc in contrast to the normal of 0.2–0 4 micrograms Recently Sjoerdsma and his co-workers described a simple test for the diagnosis of metastasizing carcinoids

Mental and emotional distress may induce or aggravate dyspnea in patients with compensated or medically controlled heart disease Adverse psychogenic factors may provoke sighing respiration and/or hyperventilation

Also in emotionally unstable persons one may hear complaints such as "I cannot take a deep enough breath." Difficulty of this type may occur during night. As trivial a matter as lying on the left side and consequent awareness of heart beats may create anxiety and consequent dyspnea in some persons. In the category of incentive psychogenic causes belong psychoneurosis, hysteria, anxiety states, emotional unrest and stress, fear, apprehension, sense of inadequacy and frustration. Hyperventilation leads to excessive elimination of carbon dioxide with consequent alkalosis and air hunger. It is associated with faintness, dizziness, giddiness, even with syncope. Tightness in the chest, choking sensation, palpitation, paresthesia (numbness, tingling sensation) in the extremities may occur. Headache, cold, clammy hands, increased sensory perception (visual, olfactory, hyperesthesia of skin), twitching of the eye lids, lips and hands are of common occurrence. For this reason conventionally this condition is designated as hyperventilation syndrome.

Hyperventilation may be observed as an aura or as a seizure equivalent of epilepsy, mostly of focal epilepsy. Also it is known that fever may cause hyperventilation. The latter may also be provoked by exertion in cardiac and extensive pulmonary disease.

In the category of miscellaneous causes of dyspnea the following items should be mentioned: pulmonary hyaline membrane formation, thiamine chloride deficiency, macroglobulinemia, depression of the carbonic anhydrase content of the blood, protein deficiency in malnutrition. The enzyme carbonic anhydrase is instrumental in releasing carbon dioxide in the lung. Failure of this enzymatic action results in retention of carbon dioxide and dyspnea. Dyspnea with pain in the chest may be the first symptom of pulseless disease. Hypoproteinemia may lead to shortness of breath because of lack of sufficient hemoglobin, decreased blood volume and subliminal edema of the alveolar capillary membrane. In severe preeclampsia and eclampsia one may observe laryngospasm, labored breathing with a respiratory rate less than 10 per minute. In 1950 Keeton and his associates reported the occurrence of severe dyspnea following abrupt withdrawal of ACTH in patients with pulmonary fibrosis and emphysema. Contrast medium used in angiocardiography may cause sudden pulmonary edema and thus severe dyspnea. Administration of 100% oxygen to emphysematous patients with pronounced dyspnea and acidosis is followed by increased shortness of breath. The reason for this adverse seemingly paradoxical response is that in these individuals hypoxia is the sole stimulant of the respiratory center. With sudden correction of hypoxia the function of the respiratory center is lessened or its complete cessation results in fatal termination. Morphine is bound to aggravate respiratory distress when given during asthmatic attacks. It not only depresses the respiratory center but also intensifies bronchospasm. According to Paton, morphine is a histamine liberator. Morphine given to patients with myocardial infarction may cause Cheyne-Stokes respiration. The latter may be observed in cardiovascular diseases and in extensive severe liver disease.

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CHAPTER 3

The Evaluation of Pulmonary Function in Clinical Practice

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INTRODUCTION

In the last few years there has been great progress in the application of physiologic studies in patients with pulmonary diseases. A background of basic pulmonary physiology is essential to a full comprehension of the contributions of these practical technics in the study of the patient with lung disease. However, a great deal of information about the patient is available to the general physician without the necessity of obtaining special and expensive studies. It is the purpose of this chapter to describe clinical methods and simple physiologic procedures which are available to any physician and require little special skill to interpret. Some of the methods which are available in specialized laboratories will be mentioned briefly but for a full discussion of them the reader is referred to read some of the recent excellent publications devoted specifically to pulmonary physiologic technics.[1-4]

I. FORMS OF PULMONARY INSUFFICIENCY

Table I gives a simple classification of the forms of pulmonary insufficiency. This classification is incomplete and over simplified but it is helpful for organizing one's thoughts about the problems encountered in patients. Obstructive ventilatory insufficiency is due to limitation of ventilation by generalized partial obstruction of the bronchioles. Restrictive ventilatory insufficiency, on the other hand, is

TABLE I

Classification of Pulmonary Insufficiency

Type	Diseases
I Defects in Ventilation	
A Obstructive	
1 Partial Bronchiolar Obstruction	Bronchial asthma, Bronchitis, emphysema
2 Loss of pulmonary elasticity	Emphysema, advanced age
B Restrictive	
1 Neuromuscular	Poliomyelitis, myasthenia
2 Chest wall limitation	
a Skeletal	Kyphoscoliosis, Marie-Strumpel arthritis
b Pleural	Pleural fibrosis
3 Pulmonary	Diffuse fibrosis, Miliary granulomata
4 Pulmonary Collapse	Spontaneous or traumatic pneumothorax
II Defects in Gas Exchange	
A Diffusional	Interstitial fibrosis, Sarcoidosis
B Distributive	
1 Uneven Ventilation	Emphysema, chronic bronchitis and bronchiolitis
2 Uneven Circulation	Emphysema
C Circulatory	
1 Acute	Massive pulmonary embolus
2 Chronic	Thrombosis of pulmonary artery

due to limitation of pulmonary expansion which may be intrinsic or extrinsic

The term diffusional insufficiency is used to denote a defect in gas exchange due to a thickening of the alveolo capillary membrane Distributive impairment indicates unequal ventilation to various parts of the lung due to varying degrees of obstruction of smaller bronchi This is most commonly seen in pulmonary emphysema with an element of chronic bronchitis Uneven circulation similarly may occur with variation in blood flow to different regions of the lung The circulatory changes are probably largely secondary to differences in pressures throughout the lungs because of varying degrees of obstruction to airflow

In most cases of diffuse pulmonary disease more than one form of functional impairment is present The best example is emphysema where all forms of impairment have been found although obstructive and distributive ventilatory insufficiency are the most prominent Pulmonary fibrosis also frequently produces multiple physiologic defects with much variation in the manifestations from case to case depending upon the anatomic location of the fibrous tissue

II DYSPNEA, General

Dyspnea is the most common symptom of impairment of pulmonary function Often however this is not the primary complaint of the patient and must be brought out by the general review of systems Regardless of whether dyspnea is the primary complaint or is elicited it should be investigated by further questioning to elucidate its genesis The great majority of such patients can be adequately evaluated by the general physician in the office if attention is given to a few points of history and to the simple measurements to be described in this chapter In an occasional patient more detailed testing in a cardio pulmonary laboratory may be needed

The presence of dyspnea in a given patient must be evaluated in relation to the over all picture which the patient presents Detection of gross difficulty in breathing at rest presents no problem in the young or the old On the other hand what is normal respiratory ability for a man of 80 would be rather severe functional disability for a man of 20 For this reason questions should be phrased so that the patient may relate his capabilities at exertion to those of his colleagues of similar age It is usually quite simple to differentiate those patients who use the term "short ness of breath" to indicate what is actually a general fatigability rather than true dyspnea

III DYSPNEA DUE TO NON-PULMONARY CAUSES

The following diseases are associated with a sensation of dyspnea and should be ruled out before any detailed studies of pulmonary function are undertaken

A CONGESTIVE HEART FAILURE

This is by far the most important distinction that must be made The problem is not that patients with heart disease are mistakenly thought to have pulmonary disease but rather that patients with dyspnea due to pulmonary insufficiency are misdiagnosed as having dyspnea of cardiac origin Patients with pulmonary emphysema are all too often diagnosed as having "arteriosclerotic heart disease" simply on the basis of dyspnea and age If the possibility of the dyspnea being due to pulmonary insufficiency is kept in mind the differentiation really presents little difficulty The greatest single guide in making the differentiation is the observation of the vital capacity and the speed of its expiration The cardiac patient s vital capacity may be reduced but he expels it readily while the patient with pulmonary emphysema expels it slowly and with difficulty (see below)

B ANEMIA

Dyspnea may be the principal symptom of severe anemia The hemoglobin is usually below 7 gm per 100 ml before dyspnea is noted

C HYPERVENTILATION

Patients who have hysterical reactions to certain stressful situations may complain of air hunger They often state I don t get any good out of the air I breathe Further questioning usually reveals that the dyspnea is accompanied by dizziness (giddiness) faintness and by a tingling sensation of the hands In extreme cases carpopedal spasm may be noted Deep sighs are usually evident during the examination Association with situations of emotional stress is an important part of such a history but may be brought out only by careful questioning

D OBESITY

Patients who must carry excess weight through their daily activities frequently complain of dyspnea on exertion Simple tests can be done to differentiate this form of shortness of breath from that due to lung disease In addition excessive obesity is occasionally associated with marked cyanosis which is apparently due to hypoventilation Pulmonary function is usually adequate and the deficit in respiration may be of central origin

E AIRWAY OBSTRUCTION

The presence of a tumor in the neck larynx or mediastinum may obstruct the flow of air sufficiently to cause dyspnea The patient usually notices an audible whistle of air by the narrow point in the airway especially when the rate of flow is increased as during exertion The stridor can easily be detected by auscultation over the midline Some of the causes for such obstruction are enlarged thyroid especially with substernal extension malignant tumors in the mediastinum aortic aneurisms thymic tumors tracheal and laryngeal tumors

IV EVALUATION OF DYSPNEA OF PULMONARY ORIGIN

A ROUTINE OFFICE PROCEDURES

1 *History*

After the causes of dyspnea mentioned above have been considered and eliminated the physician should elicit information from the patient to differentiate the various causes of dyspnea directly related to the lungs and thorax

a In the Absence of Wheezing The absence of wheezing indicates that acute bronchiolar narrowing is not the cause of the dyspnea Dyspnea without wheezing is seen in pulmonary emphysema without bronchitis and in patients with restrictive and diffusional defects It is helpful to ask the patient about any shortness of breath that he notices in the process of doing his daily activities and to assess how strenuous these activities are Some persons deny significant dyspnea because they have learned that they can no longer tolerate even moderate exertion They may have gradually contracted their activities to fit their functional capacity Knowledge of such functional defects is still of importance in evaluating a patient fully however Minor degrees of dyspnea can frequently be elicited by asking the patient about his tolerance for climbing stairs hunting golf mowing the lawn shoveling snow gardening etc His ability to keep up with others of his own age in such activities constitutes very valuable information

b Dyspnea Accompanied by Wheezing Expiratory wheezing simply indicates partial bronchiolar obstruction but gives no information as to the cause of the bronchiolar narrowing Allergic bronchial asthma is characteristically paroxysmal in nature and associated with allergens which can usually be found by careful search Between attacks the asthmatic patient is free of dyspnea whereas

the patient with pulmonary emphysema suffers from exertional dyspnea even between the acute episodes Paroxysmal dyspnea with wheezing limited to late summer and autumn usually indicates an allergic asthma due to pollens In a farmer allergy to the dusts encountered in and around the barn may produce symptoms the year around when he is exposed to these allergens Symptoms may be severe enough to make it necessary for such a person to leave the farm permanently

The patient with diffuse pulmonary emphysema may develop wheezing respirations at any time of the year in association with an acute episode of bronchitis These attacks are not associated with any demonstrable allergen and the bronchiolar narrowing is caused by mucosal edema and an increase in the bronchial secretions due to the infection As stated above this type of patient is never really free of exertional dyspnea even during periods between acute exacerbations

The past medical history may furnish very valuable information for understanding the clinical problem A history of pleural infection chest trauma or rheumatoid spondylitis directs attention to restriction of motion of the chest wall Previous work with silica dust asbestos beryllium or other such materials directs attention toward pulmonary fibrosis

Inquiry should also be made into the social and emotional problems of the patient Anxiety may suggest hyperventilation as the cause of symptoms The prospect of industrial compensation may color the picture considerably and information on this aspect of the case should be considered

2 *Physical Examination*

A distinction must be made at this point between the patients whose presenting complaint is dyspnea and who manifest the symptom at the time of the examination and those whose chief complaint is not so straight forward and in whom study of pulmonary function must be undertaken to help in fully understanding the clinical problem In the presence of dyspnea at the time of the examination one may observe its character at first hand When the subject is not dyspneic at the time of the examination a more detailed study is necessary to evaluate the extent to which an impairment of pulmonary function contributes to the over all clinical picture

a **In the Presence of Dyspnea** Deep slow unlabored respiration indicates either metabolic acidosis (Kussmaul breathing) or hyperventilation due to anxiety in neither of which is the lung primarily implicated Rapid shallow respiration may result from cardiac failure pneumonia with pleural pain pulmonary infarction severe limitation of chest wall motion or massive pleural effusion Noisy labored respiration results from multiple points of obstruction of air flow and the presence of mucus in the bronchial tree Greater obstruction occurs in expiration and this phase is therefore prolonged The patient will often state that he has difficulty in getting enough air in but objective observation will show that he is unable to expire rapidly or completely so that he is taking each breath without having completely expired the previous one This results in over inflation of the lungs and a sensation of limitation of inspiration

The differentiation between a patient with acute asthma from one with chronic obstructive emphysema with a superimposed infection is best made from the history In general acute asthma is characterized by a dry musical chest without rhonchi and coarse rales while the infected emphysematous lungs have a great deal of mucus which contributes noise in addition to the wheezing The asthmatic patient may occasionally have excess mucus and even mucous plugs in the bronchi In such cases the history must be relied upon for differentiation

b **In the Absence of Dyspnea at Rest** The detection of the causes of lesser degrees of dyspnea which one cannot observe first hand as part of the physical examination requires more time and skill

c **Restricted Lung Expansion** Intrapleural fluid or pleural fibrosis may limit the expansion of the lungs Both are easy to detect (although not to differentiate) on x ray Diffuse pulmonary fibrosis also can usually be seen on the roentgenogram Limitation of expansion due to neuromuscular or skeletal

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diseases affecting the chest wall requires careful physical examination for diagnosis A defect in thoracic expansion is easily seen by having the patient take a few deep breaths while one observes the motion of the bare chest It is helpful to place one hand on each side of the chest while the patient takes a deep breath and expires it fully Significant unilateral limitation can be seen easily by comparison of the motion of the two sides of the chest in the same manner

With all of these conditions except muscular weakness the speed of both inspiration and expiration is normal and only the depth of the breath is limited The more severe degrees of impairment are detectable on gross inspection but less marked cases must be studied by some of the tests to be outlined below

d Generalized Partial Bronchiolar Obstruction High pitched sibilant sounds (wheezes) may be heard throughout the chest during expiration but they may be absent even in the presence of considerable generalized partial obstruction

The abnormality which is most diagnostic of generalized partial obstruction is a slowing of expiration This is often detectable when the patient expires a full breath as rapidly and completely as he can There may also be an easily audible noise associated with forced expiration These sounds are created by the *turbulence of air passing the multiple points* of partial obstruction and mucus within the bronchial tree

The patient who suffers from paroxysmal *allergic bronchial asthma but who is in remission* at the time he is examined frequently shows scattered expiratory wheezes but his expiration is not usually slow The patient with generalized obstructive emphysema who has no superimposed infection at the time of examination may show only scattered wheezes also but the expiration is still obviously slow The differentiation of the asth*matic patient in an attack from the patient with* mild emphysema with a superimposed bronchitis is best done by history as already discussed Regardless of the cause of the generalized bronchiolar obstruction the response to the broncho dilators may be most gratifying but of no diagnostic significance

e Impaired Diffusion When this defect exists in pure form more detailed study is needed than one can do in the office The patient should be referred to a cardio pulmonary laboratory The clinical manifestations are dyspnea and cyanosis in the absence of a significant ventilatory defect

B METHODS OF EXAMINATION BY TESTS THAT SHOULD BE AVAILABLE IN THE OFFICE

1 *Vital Capacity*

From the discussion above it is obvious that the assessment of pulmonary ventilatory ability requires measurement of both the amount of air that the patient can take into his lungs and *speed of expiration* This can be done very easily in the office without complex or expensive equipment The McKesson Scott vitalometer (Fig 1) is quite satisfactory for this purpose and is no more expensive than a sphygmomanometer The patient is asked to inspire as fully as possible first and then with the nose held closed by the examiner to expire as fully and as rapidly as possible into the instrument The test should be repeated three times to make sure that a maximal effort is obtained and that at least two of the trials check within 200 cc A note should be re*corded in parentheses after the quantity to* indicate the speed of expiration One may simply use "fast "moderate" "slow" and "very slow to indicate this factor Thus a vital ca*pacity of 4 0 liters (fast) would be a normal* result while 4 0 liters (slow) would indicate an appreciable degree of bronchiolar obstruction without impairment of the vital capacity A value of 1 8 liters (fast) indicates restriction of lung expansion without significant bronchiolar obstruction while 1 8 liters (slow) indicates restriction of total expansion plus a significant degree of diffuse bronchiolar nar*rowing* The two examples given with the notation of "slow both indicate bronchiolar narrowing but this fact would not be indicated without the inclusion of a note on the speed of expiration The patient with a vital capacity of 1 8 liters (fast) may be quite asymptomatic except for heavy exertion while

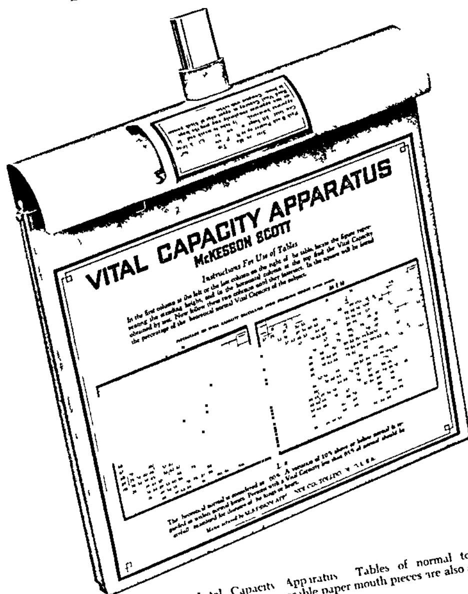


Fig. 1. McKesson Scott Vital Capacity Apparatus. Tables of normal total vital capacity are printed on the apparatus. Disposable paper mouth pieces are also available.

one with a vital capacity of 4.0 liters (slow) may be dyspneic on mild exertion. Observation of the speed of expiration gives a much better insight into the patient's respiratory problem than does the simple total quantity of the vital capacity. Such a test should be as much a part of a complete physical examination as the measurement of the systolic and diastolic blood pressures. The expected total vital capacity varies with body size and is greater in men than in women. A satisfactory table for the prediction of the vital capacity is printed on the front of the McKesson Scott Vitalometer.

2. *Timed Vital Capacity and Spirometry*

Where equipment is available the above assessment of ventilatory capacity can be quantitated very easily. Both a recording spirometer and the Collins Timed Vitalometer (Fig. 2) as described by Gaensler in 1951 are satisfactory instruments for this purpose. The



Fig 2 Gaensler Collins Vitalometer The one second and total vital capacity values are indicated on the dial by separate indicator hands

Timed Vitalometer requires much less time and experience than does the use of the recording spirometer and is cheaper The Timed Vitalometer indicates the total amount of the vital capacity and the portion which is expelled in one second (by means of a timing solenoid) Thus one obtains two figures for each vital capacity this takes the place of the rough quantitation of the speed of expiration and is much more meaningful One may record the one second and total vital capacity together separated by a slash mark just as one usually records the systolic and diastolic blood pressures Thus a recording of 1 4/3 2 liters indicates a 1 second value of 1 4 liters and a total vital capacity of 3 2 liters The patient without diffuse bronchiolar narrowing should expire 80% or more of his total vital capacity in the first second A patient whose one second value is below 80% of his total vital capacity has diffuse bronchiolar narrowing regardless of the total vital capacity Just as

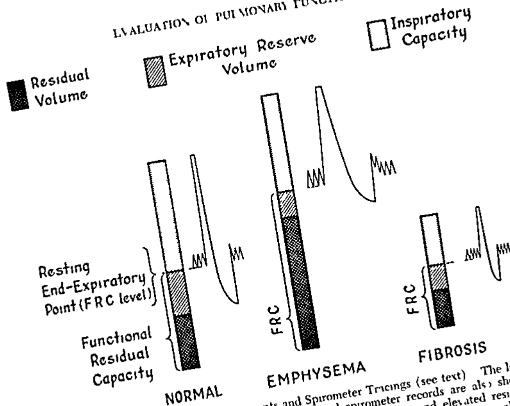


Fig 3 Lung Volume Compartments and Spirometer Tracings (see text) The lung compartments are indicated by the bars Typical spirometer records are also shown (read left to right) The slow expiration of the vital capacity and elevated residual capacity of emphysema stand out in contrast to the rapid expulsion of a smaller volume of air in pure pulmonary fibrosis

was noted in the previous discussion of the rough assessment of the speed of expiration a patient with a vital capacity of 1 0/4 0 liters would by symptomatic on mild exertion and one with a value of 2 0/2 2 liters might well be dyspneic only on heavy exertion

The use of the timed vital capacity (1 second) enables one to get essentially the same information that would be obtained by the performance of a Maximum Breathing Capacity and other tests which require much more equipment and the services of someone trained in its use A little reflection will show the obvious truth of this since the Maximum Breathing Capacity requires multiple rapid expirations and it is only the quantity expired rapidly that is measured Gaensler has found a very high correlation between the one second vital capacity and the Maximum Breathing Capacity

The recording spirometer gives similar information Figure 3 shows a portion of a normal tracing with recording of the tidal volume during resting breathing followed by a vital capacity The speed of expiration is indicated by the slope of the tracing It slows only at the end of expiration The patient with emphysema shows a more gradual slope during expiration with greater slowing as expiration progresses The vital capacity effort is seen to be followed by a period of air trapping with breathing temporarily at a higher level of lung inflation In pulmonary fibrosis the tracing shows more rapid breathing with smaller tidal volume and marke limitation of the vital capacity The speed o expiration is not impaired

3 *Exercise Tolerance*

Just as the tolerance for physical exerti is the key point in the history for judging functional state of the lungs so is the use a somewhat standard exercise an impor part of the physical examination Var step tests have been described but the cise we have used is one that is readily



Fig 4 Inspiration Expiration Films of a Normal Adult Male *Left* Inspiration film *Right* Expiration film of same patient with inspiration film tracing showing the extent of motion of the diaphragm and chest wall *Note the relatively equal motion of the two sides both as to rib cage and diaphragm*

able in almost any office or hospital A satisfactory *routine is to take the patient for a* walk without specifically telling him that his pulmonary function is being tested One may go down a hall up one or two flights of stairs in the course of the walk and then back to the office Observation of breathing during and at the conclusion of the walk is not sufficient because it may be misleading One should use the patient s ability to carry on a conversation in which he is encouraged to do most of the talking as the indication of the onset of dyspnea An anxious patient or one who is seeking compensation may state that he is dyspneic if he is asked while a stoic individual may deny shortness of breath because of a desire to deny illness For this reason it has been found that the ability of the patient *to talk is of great value Talking requires* slow controlled expiration gauged by the needs of the larynx to produce the desired sounds and not gauged by the needs for excretion of carbon dioxide This means that one must have some breathing reserve in order to continue to speak If the demands for the excretion of carbon dioxide become primary (as in severe exercise in the normal or moderate exercise in those with impaired *pulmonary function and even rest in those with* severe impairment) speech will be in gasps using short phrases between quick breaths rather than complete sentences The patient may not be aware of real dyspnea but the experienced physician can detect it by observing the speech during such a mild exertion as walking and stair climbing A normal person can talk continuously up two or more flights of stairs The neurotic patient who feels he is *dyspneic on exertion may talk incessantly* about his problems in his work or home life or trouble in getting compensation for his illness while performing such a test This simply indicates that one should look elsewhere than his lungs for such a patient s primary disease

4 Fluoroscopy and Roentgenography

Chest wall and diaphragmatic motion can easily be determined and permanently recorded by taking a standard film in full inspiration followed by one in full expiration One can see the degree of expansion of the *lungs very easily by superimposing the ex*piration film over the one taken in inspiration

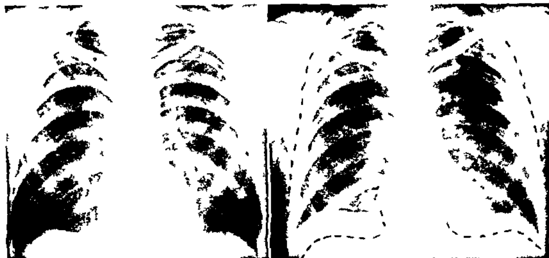


Fig 5 Patient with Pulmonary Emphysema (and right upper lobe tuberculous infiltrate) *Left* Inspiration film *Right* Expiration film of same patient with inspiration film tracing showing the marked bilateral limitation of motion of diaphragm and ribs Contrast with the degree of motion in Figure 4

and outlining on the former with a wax pencil the chest wall and diaphragm levels seen on the inspiration film (Figs 4 5 and 6) To align the films one should superimpose the transverse process of the first two thoracic vertebrae and not the clavicles The clavicles move as part of the chest wall motion and one must use the upper vertebral structures as fixed points Shifts of the mediastinum due to bronchial obstruction or to fixation of one hemithorax can also be easily detected by this method This method contributes no information on the ease of ventilation but only on the total excursion achieved

The same information can be obtained by fluoroscopy taking into account diaphragm and chest wall motion and shift of the mediastinum on deep breathing In addition paralysis or paresis of a hemidiaphragm can be detected by asking the patient to "sniff" or to draw a quick short breath through the nose while the two leaves of diaphragm are being observed Sometimes a weak hemidiaphragm will appear to move when the patient takes an ordinary deep breath but paresis can be brought out by creating a greater negative intrathoracic pressure by means of a "sniff" With this increase in negative intrathoracic pressure at the same time the diaphragm is contracting a normal diaphragm will move downward and a weak one will move upward (paradoxical motion) because of the sharp rise in negative intrathoracic pressure

5 *Carbon Dioxide Combining Power*

This chemical determination of the free bicarbonate in venous blood is available in most hospital laboratories It is most commonly thought of as a procedure of value in the detection of *metabolic acidosis* in which case it is low (below 20 milliequivalents/liter or 45 vol %) and *metabolic alkalosis* in which it is elevated (above 30 Meq/liter or 65 vol %) However it is of great value in detecting respiratory acidosis due to the accumulation of carbon dioxide In a patient who has symptoms of respiratory insufficiency an elevated carbon dioxide combining power indicates *respiratory acidosis* with CO_2 retention [illegible] On the other hand in a patient with hyperventilation a low CO_2 combining power and no metabolic cause for acidosis it is likely that he has *respiratory alkalosis* due to excessive elimination of carbon dioxide It is in patients whose carbon dioxide combining power is elevated due to carbon dioxide retention that it is dangerous to give pure oxygen therapy because they are dependent upon the stimulus of anoxia rather than the carbon



Fig 6 Patient with Unilateral Ventilatory Impairment due to Previous Pleurisy with Effusion *Left* Inspiration film *Right* The inspiratory outlines of rib cage and diaphragms have been traced on the expiration film The left diaphragm shows moderate limitation of excursion while the right side moves normally

dioxide tension as in normals to maintain respiration

6 *Electrocardiogram*

The presence of the pattern of right ventricular strain on the electrocardiogram in a patient with chronic pulmonary symptoms indicates a diagnosis of severe pulmonary insufficiency with pulmonary hypertension The carbon dioxide combining power of the blood is usually elevated in such patients as another indication of severe respiratory insufficiency It is important to recognize the picture of cor pulmonale in a patient with cardiac failure because routine measures for the relief of the symptoms of heart failure are much less effective in such patients The acute episode of right heart failure is usually precipitated by an exacerbation of bronchitis and therapy should be directed toward the relief of the bronchial infection Isuprel and neomycin given by aerosol accomplish good bronchodilatation and give local antibiotic effect In combination with systemic penicillin this therapy usually controls the bronchial infection satisfactorily These patients are frequently afebrile even in the presence of a disabling bronchial infection The cough may produce little sputum because it is so weak One must rely on the finding of respiratory distress the slow expiration the appearance of the electrocardiogram and the elevated carbon dioxide combining power to make the diagnosis

C METHODS AVAILABLE IN CARDIO PULMONARY LABORATORIES

One occasionally encounters a pulmonary function problem which is too complex to understand by the methods available in the office Most large cities now have well equipped laboratories where function can be evaluated in much greater detail Since there are such excellent and recent monographs on these technics they will not be taken up in detail here The authors feel that the purpose of this section on the evaluation of pulmonary function is to emphasize how much can be learned in the office without complex and expensive tests and will leave it to the interested reader to look elsewhere for the details of the tests to be mentioned below By the procedure available in the office one evaluates very little more than ventilatory ability but for most

cases this is adequate. There is good correlation between impairment in ventilatory function and abnormality in the tests to be mentioned. In the authors' research laboratory, for instance, most of the tests to be listed are available and yet the procedures available in any office are used for the evaluation of the great majority of patients both in internal medicine and in preoperative studies. It is on the usefulness of the simple procedures discussed above that the authors wish to place emphasis.

1 *Lung Volumes*

The subdivisions of the total lung volume are shown in Figure 3. The basic determination to be made in the laboratory is the "functional residual capacity." This may be done by the nitrogen washout method (open circuit method)[6] by helium dilution, or by the use of a body plethysmograph.[8] The expiratory reserve volume, inspiratory capacity and vital capacity are determined on a recording spirometer. By subtracting the expiratory reserve volume from the functional residual capacity one obtains the "residual volume" of the lungs. This value should not exceed 35% of the total lung capacity. A residual volume of more than 35% of the total lung capacity usually indicates the presence of pulmonary emphysema, although temporary increases in the residual volume are also found in patients with acute bronchial obstruction. In most instances of an increased residual volume the situation can be strongly suspected from observing the speed of expiration of the vital capacity and particularly from the one second and total vital capacity values.

2 *Index of Pulmonary Mixing*

As part of the open circuit residual volume determination the concentration of nitrogen remaining in the alveolar air after the patient has breathed pure oxygen for 7 minutes is usually measured. Normally the nitrogen concentration in alveolar air is reduced to 2.5% or less in this period of time, but with various degrees of trapping and uneven ventilation which occur in emphysema one may find nitrogen of 8 to 12% in the alveolar air. Such values are indicative of considerable emphysema and a resultant poor pulmonary mixing of gases.

3 *Maximum Breathing Capacity*

The subject breathes as deeply and as rapidly as he can either through a venturi tube into a spirometer or into a collecting bag for an accurately timed period of 10 to 20 seconds. The value is expressed in liters per minute. This is the most widely used single test of pulmonary function outside of the vital capacity but it requires special equipment and considerable experience. The normal values depend upon the method used and must be established by each laboratory for its method. Recent work has shown that water filled spirometers are inadequate as test instruments. The test has many disadvantages, the greatest of which would seem to be the great subjective element which is inevitably present. Considerable cooperation on the part of the patient is necessary for a valid test. Furthermore, physical weakness may cause the patient to tire and give a low value even in the absence of primary pulmonary disease. The same may be said for the exercise tolerance test, but when either is used in conjunction with the timed vital capacity, physical weakness can usually be differentiated from dyspnea caused by pulmonary disease.

4 *Expiratory Air Velocity*

A number of methods have been published recently on the velocity of expiratory gas flow. These are all refinements of the timed vital capacity discussed above.

5 *Arterial Blood Examination*

Arterial blood may be obtained readily from the brachial or femoral artery under anaerobic conditions. The degree of saturation of hemoglobin, the carbon dioxide content and pH are then readily determined in a suitably equipped laboratory.[9] Methods are also available for determination of the tension of oxygen and of carbon dioxide in arterial blood.[10,11] Hemoglobin unsaturation and elevation of the carbon dioxide tension are common findings in pulmonary emphysema. Again these abnormalities can be strongly and fairly accu-

rately suspected by the intelligent use of the methods available in the office

6. *Ear Oximetry*

Arterial blood hemoglobin saturation can be estimated by the use of an oximeter without resorting to arterial puncture The saturation is measured at rest on room air, during exercise, and during breathing of 100% oxygen Normally one should maintain a hemoglobin saturation over 95% on room air and this should remain the same or rise with mild exercise In patients with severe emphysema and with impaired diffusion the saturation on room air is usually low and may fall during exercise

7. *Diffusion Capacity*

An occasional patient has a degree of cyanosis which seems out of proportion to the degree of ventilatory incapacity This may indicate congenital heart disease with a right to left shunt, or a block of gas diffusion between the alveoli and the capillaries A defect in gas diffusion may be detected by the method described by Riley in which arterial blood oxygen tensions are determined while the subject breathes gas mixtures with two different known oxygen tensions[13–15] Ordinarily there should not be more than 11 mm Hg difference in the oxygen tension of the alveoli and the arterial blood A greater difference while breathing the low oxygen mixture indicates that the diffusion from alveolar gas to pulmonary capillary blood is impaired Diffusion may also be evaluated by techniques employing low concentrations of carbon monoxide as the test gas

8 *Bronchospirometry*

In instances of disease in which one lung has been affected more severely than the other, it may occasionally be desirable to determine the functional status of the lungs separately A patient may have nearly normal total function even in the presence of moderately severe impairment of one lung For this type of study a double lumen catheter is introduced into the trachea The two lumens are of different lengths, the longer is placed in the left main bronchus and the shorter remains in the trachea The trachea and left main bronchus are occluded by inflated balloons This permits the ventilation of the two lungs to be separate and it can readily be measured with a double spirometer The lungs can be evaluated separately as to ventilation, oxygen consumption, vital capacity, etc The interested reader is referred to the excellent review of bronchospirometry by Gaensler[18 19]

9. *Cardiac Catheterization*

This method has been a useful research tool in gaining an understanding of the effect of pulmonary disease upon the function of the heart[12] The principal effect of chronic pulmonary disease upon the circulatory system is the development of hypertension in the pulmonary artery This is followed by right heart failure (cor pulmonale) if it is severe and persistent An increase in pulmonary blood pressure should be suspected when one hears a pulmonic valve second sound that is louder than the aortic valve second sound, in a patient with pulmonary disease When right ventricular hypertrophy or strain is demonstrable on the electrocardiogram in such a patient, one can be sure of a significant degree of pulmonary hypertension without resorting to cardiac catheterization

10. *Determination of Mechanics of Breathing*

Of all the studies that have been done in a cardio pulmonary laboratory, perhaps the one that has contributed the most to the understanding of the basic physiologic defect of pulmonary emphysema and fibrosis is the determination of the relationship between the pressure existing within the chest and the flow of air into and out of the lungs Pulmonary volumes are determined by means of a spirometer, gas flow rates by a pneumotachygraph gas flow meter, and the intrathoracic pressures by means of a plastic tube which is passed into the esophagus through the nose[21]

By measuring the pressure within the chest at various degrees of lung inflation (with no air flow) one can evaluate the elasticity of the lungs (the reciprocal of this value is referred to as compliance) From these data one can determine a pressure-volume curve for the lung, just as the physicist determines this

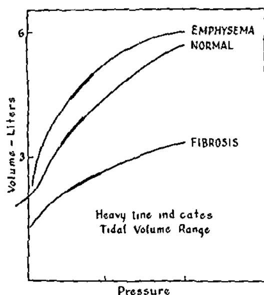


Fig. 7 Volume-pressure Curves (Compliance) (For explanation see text.)

relationship for various materials. Figure 7 shows the pressure volume curves for a normal individual, for a patient with pulmonary emphysema and for a patient with pulmonary fibrosis. The slope of such a line is expressed as the elasticity and it can be seen to be nearly straight in the range of the tidal volume.

The pressure measured during active breathing includes also the pressure necessary to overcome resistance to air flow and change in volume of the lungs. If the elastic pressure is subtracted, the pressure related to resistance to air flow is found. The relationship between this pressure and the flow of air is shown in Figure 8 for the normal and also for a patient with pulmonary emphysema. The limitation of the rate of gas flow in the patient with emphysema is quite evident and it is of further interest that an increase in the positive pressure exerted upon the lung by such a patient does not result in an increased rate of expiratory flow. This is evident when one has such a patient make a forced expiration for the determination of the vital capacity. In the latter part of a forced expiration the patient pushes exceedingly hard but

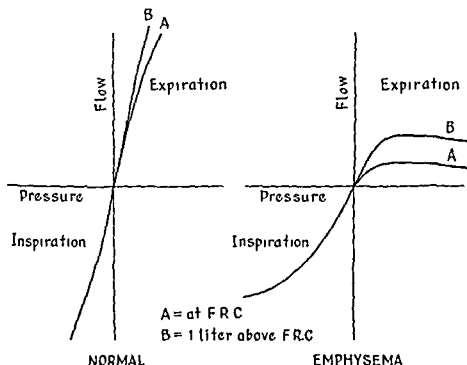


Fig. 8 Flow pressure Curves indicating breathing resistance. (For explanation see text.)

accomplishes only a very slow exhalation

The normal individual has been found to have a pulmonary compliance of .2 liters per cm water pressure This means that when a pressure of 1 cm of water is applied the lung (independent of the thorax) will increase in volume by 200 cc Since compliance is the reciprocal of elasticity, a lung of high compliance has a low elasticity (is easily stretched) while a lung with a low compliance (stiff lung) has a high elasticity The term compliance is used more commonly than elasticity in the literature

It is easy to see from studying the figures that the patient with emphysema works harder in breathing than does the normal His lungs are distended toward the top of their capacity (they are stretched out) and he has an increased resistance to expiratory air flow [8]

Unfortunately these studies have not solved the knotty problem of where the primary defect lies in the pathogenesis of emphysema but they have shed considerable light upon the physiologic defect that characterizes the disease

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CHAPTER 4

The Common Cold

HAROLD S DIEHL MD

THE COMMON cold continues to be the leading cause of illness in our country and to produce an enormous amount of disability and loss of time from usual activity. According to a survey conducted by the American Institute of Public Opinion during the week of January 12 1936 28½ million persons in the United States—nearly one person in five—were afflicted with colds. In a large series of families in Cleveland Ohio Dr John Dingle and colleagues found over a 9 year period that respiratory diseases account for two thirds of all the illnesses in these families and that colds are much the most frequent type of respiratory illness. They found also that 15% of the individuals in these families get a new cold each week during the winter months and that the average incidence of acute respiratory infections is 6.5 per person per year with the highest rate among children under six years of age[1]

Reports from industry indicate that the average employed person loses 2½ days a year from colds or related respiratory infections. This one group of conditions is therefore responsible for almost exactly half of all absences from work. According to estimates by the United States Public Health Service the total time lost from colds in this country amounts to 150 000 000 work days annually. In loss of wages and production and in costs of drugs and medical and hospital services this adds up to the staggering total of five billion dollars annually[3]

An analysis of the results of five surveys of illness covering 97 285 full time person years of observation in widely scattered sections of the United States shows that the three leading causes of illness are (1) coryza and colds with 204 cases annually per 1 000 population (2) bronchitis with 103 cases per 1 000 population and (3) influenza and grippe with 84 cases per 1 000 population. Of illnesses causing disability of one day or longer the same three top the list but in the following order (1) influenza and grippe with 74 cases (2) coryza and colds with 59 cases and (3) bronchitis with 51 cases per 1 000 population. The total days of disability per year by cause of illness are highest for arthritis and chronic rheumatism with 934 days per 1 000 population nervous diseases are second with 770 days accidents and poisoning third with 673 days heart disease fourth with 626 days and influenza and grippe fifth with 612 days of disability annually per 1 000 population. However if one totals the days of disability from the three most common acute respiratory illnesses coryza and colds bronchitis and influenza and grippe one gets 1 219 days of disability per year per 1 000 population—a total which again puts these acute respiratory diseases at the top of the list[4]

By any yard stick therefore it appears that colds and related acute respiratory diseases rank exceedingly high as causes of illness and disability in this country

DEFINITION

It is still not possible to give an entirely satisfactory definition of the "common cold" Physicians and laymen alike apply the term to various acute sub acute and even chronic

maladies of both the upper and the lower portions of the respiratory tract.

Certain investigators have attempted to limit the application of the term "common cold" to the condition most frequently described as a "cold in the head." From a scientific point of view there is considerable justification for this attempt to simplify the problem. On the other hand acute respiratory infections rarely remain limited to one portion of the respiratory tract. A condition which is a typical rhinitis today may become a sinusitis, pharyngitis, laryngitis, tracheitis or bronchitis a few days hence. Furthermore coryza is a prominent symptom in hay fever and is exceedingly common in influenza.

In general the symptoms considered most typical of the common cold are sneezing, coryza, nasal stuffiness and a dryness or irritation of the membranes lining the nose and throat. At the onset there is usually a sensation of chilliness. At this stage body temperature is below normal and blood flow in the skin is reduced. In the early stages of an acute cold nasal discharge is profuse and watery, but in two or three days the discharge becomes thicker and mucopurulent in character. Involvement of the lower respiratory tract with hoarseness and coughing is common.

In addition to this typical picture of a common cold there are many so called "colds" which begin with a pharyngitis, laryngitis or tracheitis. Such colds frequently extend to the nasal mucous membranes producing the symptoms typical of a head cold. Slight fever may accompany acute colds although if the fever is high one should suspect a more severe type of infection or some complication such as sinusitis, otitis media, tonsillitis, bronchitis or pneumonia.

Studies conducted over the past several years have resulted in the isolation and identification of several viruses which are responsible for certain of the acute upper respiratory tract infections. When the agents which cause the larger group of upper respiratory infections including the common cold can be similarly identified it will be possible to classify these infections according to etiology. Until that time accurate definition will continue to be impossible.

THE CAUSE OF COLDS

The common belief until recently, as the name suggests, was that colds are due to chilling. Observation, however, suggested that at least some colds are communicable. Hence with the development of bacteriology attention was centered upon a search for bacteria in the secretions of the respiratory tract during colds. These investigations revealed few, if any, bacteria in the nasal secretions during the early stages of the acute head cold, and these were not constant in type. On the other hand bacteria were uniformly present in the late stages of colds as well as during the initial stages of tonsillitis and related conditions.

Investigations of the etiology of the common cold have been numerous and fruitful but not entirely conclusive. A review of available information would seem to justify the following summary as to current scientific opinion concerning the cause of colds.

VIRUS

A filterable virus as a cause of colds was suggested in 1914 by Professor Kruse, Director of the Institute of Hygiene in Leipsig.[4] The experiments which Kruse conducted were briefly as follows. He collected some nasal discharge from a student who was in the initial stages of an acute head cold, mixed this with water and filtered it through a porcelain filter. The filtrate was free of bacteria. He then introduced several drops of this filtrate into the nasal cavities of 36 members of his bacteriology class. Forty two per cent of these students developed typical head colds while no colds developed among the 29 uninoculated members of the class. From this he concluded that a filterable virus is probably the causative agent in colds.

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diers as subjects repeated the experiment in this country and obtained similar results On the basis of his studies he concluded that common colds at least of a certain type are infections and that a causative virus occurs *in the nasal secretion*

World War I interrupted this line of promising investigation and it was not taken up again until 1924 when Dochez[8] and his associates at Presbyterian Hospital in New York City began to investigate this problem Their experiments which were exhaustive and carried out under carefully controlled conditions caused them to conclude that colds can be transmitted from man to the chimpanzee and from man to man by means of Berkefeld filtrates of nasal washings from individuals suffering from acute colds and that the cause of colds is a filterable agent which in all likelihood belongs to the group of so called submicroscopic viruses Shortly thereafter a group of investigators at Johns Hopkins University in Baltimore demonstrated that a filterable virus is capable of producing in man and in chimpanzees symptoms typical of an acute cold[9]

In more recent years various workers have shown that a virus is present in the nose and throat secretions of patients with colds which when introduced into the nasal cavity will produce colds in approximately 50% of susceptible individuals However investigators have been seriously handicapped in their studies by their inability either to establish *this virus in experimental animals or to culti*vate it in the laboratory

Several other viruses called adeno viruses which cause acute upper respiratory infections characterized primarily by pharyngitis and conjunctivitis have been *isolated and* cultivated as distinct entities[10] According to Dingle however these viruses are responsible for not more than 3 to 5% of acute upper respiratory tract infections in the civilian population and are clearly different from the virus or viruses of the common cold

Recently still another virus has been isolated from persons with acute upper respiratory infections by Dr Winston Harvey Price of Johns Hopkins University and one or two other investigators Dr Price has been able to cultivate this virus in the laboratory and to produce a vaccine which in a group of medical students and nurses seems to give considerable protection against infection with this particular organism As yet however we have no information as to what proportion of the acute respiratory infections i e 5 10 or 15 per cent commonly called colds are due to this virus[11]

The usual symptoms of these virus colds" in human subjects are "stuffiness of the nose sneezing watery nasal discharge dryness of the throat occasionally mild headaches and often mild general symptoms but with no elevation of temperature and a usual duration of 4 to 5 days"[12] This mild course however occurs only if the subjects are carefully isolated from all possible contact with other persons Otherwise this acute process is usually followed by secondary infection with other germs that happen to be present in the nose and throat These secondary infections usually persist two or three weeks are accompanied by a thick yellow discharge and may involve the sinuses

BACTERIA

Before the existence of filterable viruses was known competent bacteriologists had reported studies which seemed to indicate that certain bacteria were the cause of colds This work was overshadowed for a number of years by the developments concerning a virus in colds *but Thomson and Thomson*[13] *report that* 15 years of "exceedingly careful" study of the bacterial flora of the respiratory tract in a limited number of persons during health and during colds leads them to conclude that *pneumococci bacillus influenzae streptococci* and micrococcus catarrhalis are definite primary causes of colds In 1929 Walker[14] reported that a culture of micrococcus catarrhalis which had been isolated originally from a human throat but had been on artificial media for 10 years produced typical head colds in two out of three subjects who were inoculated intranasally with this culture

At the meeting of the American Medical Association in 1933 *the late Dr William Park* in discussing a paper on colds by Doctors

Dochez Mills and Kneeland said "I think that Doctor Kneeland has gone too far in denying that ordinary bacteria may start a common cold. In the big epidemic of 1918 three of my technicians were accidentally sprayed by fresh influenza cultures (Pfeiffer) and two of them developed definite rhinopharyngeal colds within 12 hours. The symptoms lasted for a few days. Cultures from their nostrils and pharynx showed the same type of bacilli that was sprayed on them. These remained prevalent for several days and then disappeared in the course of the next 2 weeks. I am one of those who believe that many persons after exposure to chilling develop a common cold. It seems to me that very contagious colds are usually due to filterable viruses. Persons have also some endogenous infections from their own organisms and some contract colds which are not due to the filterable virus." To this Doctor Kneeland replied "I think that Doctor Park is right. There is such a thing as a pure bacterial cold. Our observations on filterable viruses and our general hypothesis as to the etiology of these disorders are based on the ordinary outbreaks of highly communicable respiratory diseases."

Weighing all of these studies and opinions it seems that one must conclude that certain bacteria not only act as secondary invaders in virus colds but also may themselves be the primary cause of colds. Most of these bacterial colds seem to begin with a severe sore throat with the nasal discharge and congestion appearing later as the infection extends upward into the nasal passages.

CHILLING

It is common experience that exposure to drafts and chilling of the whole or of portions of the body may result in sneezing and nasal stuffiness and discharge. Just why these symptoms occur is not entirely clear but the probability is that they are due primarily to changes in the blood flow to the skin and mucous membranes. Experiments by Taylor and Dyrenforth[10] lead to the conclusion that chilling of the body surfaces without compensation by exercise leads to peripheral stasis and anoxemia to lowered leucocyte response and to impairment of the phagocytic capabilities of the fixed tissue cells including those of the nasal mucous membrane.

In 1921 Mudd and his associates[11] reported that chilling of the body surfaces causes a fall in the temperature of the nasal and pharyngeal mucous membranes and that this chilling and the accompanying vasomotor reaction may so disturb the equilibrium between the host and the bacteria of the nose as to favor the development of infection. Winslow and Greenburg[12] after a series of experiments on students at Yale agreed that "chilling of the body surface results in contraction and ischemia and dryness of the membranes of the nose."

These findings are confirmed and extended by the studies of Spiesman[13] which show that in individuals who have frequent colds the vasomotor response of the nasal mucous membranes to peripheral cold stimuli is much less in degree and slower in appearance than in normal persons and that during an acute cold this reaction is entirely absent.

These reactions are less likely to occur in individuals who are taking active physical exercise and have accustomed themselves to rapid changes in temperature. Illustrative of this is the experience of Arctic explorers who report that members of their party and Eskimos with whom they come in contact go all winter long without colds even though exposed to extreme and rapid changes in temperature. They pass suddenly from a temperature of 80 to 90 inside their igloos to 30 to 40 below zero on the outside. They may fall into the water and have their clothes become solid ice on them or be soaked to the skin with perspiration and shiver to keep warm and still they do not develop colds.

W. F. Kerr,[14] Professor of Medicine at the University of California expresses the opinion based upon his own investigations that colds are due primarily to failure of the body to adjust adequately to temperature changes. On the other hand Dowling Jackson and their associates at the University of Illinois have chilled people clothed and with overcoats on at 40 and with nothing on but shorts or shorts and brassieres at 60 without any effect on the occurrence of colds. From these experiments they conclude that chilling

will not of itself induce spontaneous colds

CLIMATE

Climate is believed by many to be an important factor in the development of colds. This is due largely to the fact that colds are many times as prevalent during the winter months as during the summer. Yet, this seasonal incidence occurs in the balmy South, in Rio de Janeiro, in Honolulu, and even in California, just as it does in Minnesota. Furthermore, the change of seasons does not explain the several quite distinct waves of increased frequency of colds which occur during the winter.

Analyses of the frequence of colds among the employees of the Metropolitan Life Insurance Company[22] have led to the conclusion that colds tend to increase somewhat whenever there is a distinct drop in outside temperature.

Studies conducted by the United States Public Health Service in six American cities of wide geographic and climatic differences also have shown a slight tendency for colds to increase when there is a decrease in temperature below the "norm" for the corresponding week and also for the preceding week.[23] None of these studies, however, has shown any clear cut and significant relationship between the occurrence of colds and the daily range of temperature, the humidity, the rainfall, the wind velocity, the percentage of sunshine or the atmospheric pressure.

The general belief, or at least the hope, on the part of individuals who are subject to frequent colds, is that their cold problems would be solved if they could just move to some other climate. Unfortunately, this belief finds little support in several carefully conducted studies by the United States Public Health Service of the occurrence of colds in certain student and family groups in the different parts of the country.[24] The student groups studied were from Harvard University, Mount Holyoke College, Johns Hopkins University, Georgetown University, Tulane University, University of Chicago, Ohio State University, University of Utah, University of Arizona, and University of California. The attack rates in these student groups were remarkably uniform, showing no consistent relationship to latitude, longitude, or climate. Similar studies among family groups show a surprising similarity in the frequence and the time of occurrence of colds in the various sections of the country. During the period of high incidence, the occurrence of epidemics in the several groups in widely different localities shows a remarkable time correspondence.

Barrow[25] studying colds among the students of Stanford University found the prevalence practically the same in the agreeable climate at Stanford University as it was among corresponding groups of students in New York and Massachusetts. Whether the student used sleeping porches, well-ventilated bedrooms, or poorly ventilated bedrooms for sleeping purposes did not materially affect their susceptibility. Finally, and most discouraging of all, we find that the death rates from pneumonia, the most serious complication of the cold, are the highest in those sections of the country to which most of us would be inclined to go to escape the colds which we associate with our northern winters.

PHYSICAL FACTORS

Anything that produces irritation or injury of the membranes of the nose and throat will cause sneezing, discharge, and the other nasal symptoms characteristic of colds. Usually these symptoms are of short duration unless the injury to the mucous membrane opens the way to bacterial infection. In such a case the cold may be severe and prolonged.

Many things may irritate the mucous membranes of the nose. When the autumn wind fills the atmosphere with dust, colds increase. There is also a widespread belief that colds diminish after a heavy fall of snow. Tobacco smoke irritates the membranes of the throat and nose of some people. In such persons smoking may be a factor in keeping up a low grade chronic irritation. The irritating gases of storage battery shops, garages, and chemical industries may produce congestion of the nose, and it has been demonstrated that overheated air, such as occurs in most Ameri-

can homes during the winter months predisposes to colds.

ALLERGIES

The symptoms which allergies produce in the upper respiratory tract are essentially the symptoms of an acute head cold: sneezing, nasal discharge and stuffiness and obstructions to breathing. In fact the symptoms which in late summer are attributed to hay fever are frequently called "spring colds" when the trees are pollinating and "rose colds" in the early summer.

People who suffer with allergic nasal mucous membranes periodically or continuously throughout the year are likely to think that their symptoms are due to repeated colds or to chronic sinus infection and certain studies indicate that a very high percentage of cold susceptible persons have allergies or come from allergic families. Sinus infection may develop in connection with or even as a result of an allergic nasal mucous membrane. In fact when polyps develop in the nose one can be reasonably certain that a chronic sinus infection is superimposed upon an allergic nasal membrane.[6]

After an allergic condition of the nasal mucous membrane has continued for a long time, particularly if medicated oils or similar preparations are dropped, sprayed or otherwise introduced into the nose, secondary infections are likely to develop. In such cases treatment of the infection is unsatisfactory unless the fundamental allergic condition is recognized and corrected. An allergic state is a contributory factor of sufficient importance to be considered in every case of chronic or recurrent colds or chronic sinus infection.

OTHER FACTORS

Various other non-specific factors seem to be related to susceptibility to colds in many individuals. Most important among these are malnutrition, fatigue, over-eating, lack of exercise, constipation, nervousness and poor ventilation. Spiesman and Arnold's[7] studies of a group of cold susceptible individuals indicate that their nasal mucous membranes react abnormally to chilling of the body surface and that lack of exercise, emotional disturbances and improper diets are factors which exert an unfavorable influence upon these reactions. It is difficult to measure accurately the importance of most of these factors but these and other studies indicate that they have some importance and it is logical to assume that persons who are in good physical condition will be less affected by the factors which predispose to colds than those whose physical condition is below par.

EPIDEMIOLOGY OF COLDS

FIELD STUDIES

Colds occur in every section of the world, from the Occident to the Orient, from the equator to the poles, from sea level to mountain tops. All ages are susceptible but children have many more colds than adults, with the highest attack rate in infants under 4 years of age. From this age the rate declines to a low point in the age group 15 to 24, rises from 25 to 34 and then again declines until it reaches a minimum in the age group of 55 years and over. In childhood boys have more colds than girls, but after the age of puberty women have more colds than men. Complications are most frequent and most serious in infants. The Gallup Poll survey of colds for the week ending January 12, 1956 reports that as in all previous studies farmers have the highest attack rate for colds of any occupational group, that people living in cities have slightly fewer colds than people living in small towns and rural areas, that persons in lower income brackets have approximately 60 percent more colds than do those in the higher income brackets and that the Pacific coast consistently shows fewer colds than other areas of the country.

In the Arctic

Some of the most significant observations on the occurrence of colds have been made in isolated communities which have little or no contact with the outside world During a trip up the west coast of Greenland, Heinbecker and Irvine Jones[29] noted that in certain settlements every native was the victim of an acute respiratory tract infection while in others no evidence of such infection was present Investigation revealed that in the former some contact had invariably been made with the outside world prior to their coming while in the latter group, within from 48 to 72 hours of their arrival, all the natives developed acute respiratory infections with sneezing, coughing, and spitting Farther north among the polar Eskimos, where it was certain that no outside contact had been made that year, there was never the slightest evidence of acute respiratory tract infections at the time of arrival of the expedition but within 72 hours nearly every Eskimo of the settlement developed such an infection

Paul and Freese[30] spent a year studying colds among the residents of the arctic mining town of Longyear City Spitzbergen, the world's northernmost settlement During the 7 months that this town was isolated none of the 507 residents had colds, in spite of the fact that many lived in overcrowded barracks and travelled daily through sub zero weather to work in a coal mine In May a ship arrived, one member of whose crew was just coming down with a cold Within 48 hours 25% of the population had colds and by the end of the month 75% of the residents had been affected From this they conclude that the disease is spread by direct contact that the incubation period appears to be about 48 hours, that the clinical course of the disease varies in individuals who presumably have been exposed to the same infection and that some persons seem to have complete immunity while others develop an immunity of short duration after an attack

These authors observed that trips to isolated villages during the winter months did not give rise to epidemics of colds, but that during the shipping season they did They also reported that trappers claimed that accidents such as falling into icy water were not associated with colds in the winter but were in the shipping season This suggests that when potentially infectious organisms are present in the nose and throat, chilling may be a factor in the production of colds

On one of his trips to the Antarctic, Admiral Byrd reported that following the opening of a box of clothing an outbreak of colds occurred among the members of his party after they had been out of contact with civilization and free of colds for about a year

In the Tropics

Milam and Smillie's[31] report of a year's study of colds in St John, U S Virgin Islands, indicates that colds are less common and much less severe on this isolated tropical island than in the temperature zone, but that the seasonal curve of frequence of acute colds in St John is a replica in miniature of the same curve for the United States

On the basis of their family studies in Cleveland, Dingle[32] reports that almost three fourths of common colds are acquired in the home It is the young school child who introduces most colds into the household Following this the chances are at least 50% that other children in the family will acquire colds When an adult introduces a cold into the home, the chances are only about one in five that other members of the family will acquire colds

LABORATORY STUDIES

Studies of the natural spread of colds have been supplemented by carefully planned and controlled laboratory experiments Some of these have used human subjects and some chimpanzees In one of these studies at Johns Hopkins University an observer with a gauze mask over her mouth came into close contact with several of the animals At this time the observer, the attendant and all of the animals were in good health and free from any evidence of infection of the upper respiratory tract On the day after the examination, however, the observer complained of sneezing, lacrimation, and dryness of the nose and throat, and on the following day was suffering

from a typical severe cold which lasted 2 weeks Two days after the examination two of the chimpanzees presented nasal discharge and obstruction and elevation in temperature and passed through the typical stages of the common cold No other primary infections developed and there were no secondary cases in this group of animals This incident occurring under controlled conditions suggests that a common cold may be contagious before the onset of actual symptoms It indicates also that the ordinary gauze mask does not provide complete protection against the common cold[33]

In another carefully controlled experiment by the same group of investigators 15 chimpanzees were under constant observation from July 15 to September 19 None showed any signs of a cold On the latter date the animals were placed in strict isolation in separate cages and four widely separated rooms the doors of which were locked while the attendants wore masks and gowns and scrubbed their hands thoroughly before coming into contact with the apes or their food The attendants were all examined daily for any signs of upper respiratory tract infection and all remained healthy On September 26 an individual on the second day of an acute cold prepared the meals for the apes but he neither saw the animals nor the attendants while in the kitchen or preparing the food He placed the food in the containers and then left after which the attendants came in and conveyed the food to the cages Within 48 hours five of the apes developed typical colds with nasal discharge mouth breathing slight fever and leucocytosis and two suffered from moderately severe cough The nasal discharge continued for 10 days but there were no secondary cases among the ten other apes It would appear therefore that coryza may be spread by contaminated food and that strict personal hygiene is necessary to prevent passing on the contagion[34]

At the University of California Kerr conducted a series of studies in an air conditioned room which would permit normal in-door activities for four to six persons Air flowed into this room at the rate of 66 cubic feet per minute and raised the pressure in the room slightly above normal Subjects were selected from men 21 to 40 years of age who were accustomed to have three or more colds per year but who had not recently been ill These subjects in groups of three to five lived in this room from 5 to 8 days after which a patient with a common cold of 12 to 36 hours duration joined them The subjects and the patient lived in intimate contact for 24 to 48 hours played cards together used common drinking glasses and eating utensils and even the same thermometer The subjects then remained 4 to 6 days longer under the same conditions Nineteen volunteers were exposed to the common cold in this manner and none contracted the disease In a second experiment nine subjects were inoculated with nasal washings from a patient with an acute cold Inoculations were made into the conjunctival sacs The untreated washings were used in four cases The washings were centrifuged and the supernatant fluid was used in four cases Heated washings was used in one case as a control None of these subjects developed any signs of symptoms of a cold In his conclusions from these studies Doctor Kerr says "This does not prove that no type of rhinitis is contagious but it does prove that colds are not so readily transmitted as many assert"

For a number of years the Medical Research Council of Great Britain has been conducting intensive studies of colds using human volunteers as subjects The introduction of material containing the cold virus into the nasal cavities of these volunteers has resulted in colds in about 50% of subjects Other studies show that colds can be transferred by contaminated hands or handkerchiefs Only three colds developed among thirty two healthy subjects who had been in close contact for 2 hours with persons who had typical and severe colds[35] From these and similar studies it seems that we are justified in concluding that the virus is present in the nasal discharge of patients during the first 3 or 4 days of an attack of a virus cold During this period it may be spread through the atmosphere in which the virus remains infective for about 5 hours through the contaminated hands of the patient either directly or indirectly through doorknobs

handrails, or other objects which are handled by groups of individuals Likewise, drinking glasses, cups, forks, and spoons are excellent vehicles for the transmission of the cold virus, as well as other micro-organisms, from one person to another Still unexplained, however, is the difficulty in transmitting colds under experimental conditions when they seem to be so highly communicable within family groups

COMPLICATIONS AND ALLIED CONDITIONS

The importance of colds lies not so much in the colds themselves as in their complications Of these the most common are sinusitis, otitis media, and *infections of the lower* respiratory tract such as laryngitis, tracheitis, bronchitis, and pneumonia Closely allied to colds but distinct disease entities are influenza, *tonsillitis*, pharyngitis, and other acute respiratory tract infections

Yates expresses the opinion that complications of the common cold occur only (1) when drainage from the sinuses or middle ear is obstructed by swelling the mucous membranes, (2) when virulent and potentially invasive organisms are present in the nose and throat at the time of the cold, (3) when the mucous of the nose is diluted by introducing solutions into the nose or by bathing, or (4) when the subject is in poor health

PREVENTION OF COLDS

NATURAL RESISTANCE

It has long been common knowledge that certain persons are much more susceptible to colds than others Some persons rarely have a cold, while others are subject to four or five colds each winter Smiley of Cornell University reported that 25% of the students have 75% of the colds in that institution each year Hereditary immunity or susceptibility have been suggested as the explanation for these differences Studies by Johns Hopkins investigators, however, indicate that susceptibility is not so fixed a quality as one would expect By studying the occurrence of colds among a large group of individuals over several years, they concluded that in most persons individual susceptibility varies from maximum to minimum over a period of several years

While the general factors responsible for natural resistance to colds are rather vague, there are certain definite local defenses which Nature has provided against the introduction of infection into the upper respiratory tract Most important among these are

(1) The tiny hairs or vibrissae at the entrance to the nasal passages These filter out coarse particles of the foreign material inhaled *with the air*

(2) The mucous secretion of the mem*branes lining the nose* *Tiny glands which are* located throughout these membranes are constantly producing a moist, slightly sticky, secretion which covers these surfaces This mucous film is in constant movement toward the pharynx and is renewed approximately every ten minutes It serves to warm and moisten the air as it is inhaled thereby conditioning the air for contact with the more delicate membranes of the lower respiratory tract Wright and Smith (38) report that thin sheets of air passing over these surfaces deposit at least three fourths of their bacterial content on the mucous membranes Some of these are de[illegible]

mucus to the pharynx, from which they are either expectorated or swallowed The mucus also protects the delicate membranes of the nose from mechanical injury by particles of dust which are contained in the air 'It is difficult for bacteria to find their way through an intact mucous covering The breaking of the mucous coat and the exposure on the underlying epithelium opens a portal of entry for pathogenic micro organisms "

(3) The cilia, which cover most of the

mucous membranes of the nose These cilia which are in constant motion much like fields of grain waving in the wind pick up particles of foreign material and carry them to the pharynx from which they are discharged or swallowed Dryness and medicated oils first slow and eventually stop the action of these cilia

These are the more obvious local defense measures that Nature has provided to protect us against colds and other infections intro duced through the upper respiratory tract It is important in our efforts to prevent colds that we do not destroy or interfere with these nat ural defenses

AVOIDANCE OF INFECTION

Under the conditions of modern life it is ob viously impossible to avoid exposure to colds The best that we can hope for is to reduce the degree of exposure thereby correspondingly reducing the probability of infection This can be accomplished by keeping one s distance from individuals who have colds by prohibit ing persons who have colds from any associa tion with infants by thorough washing of the hands before meals and after contact with ob jects likely to contain infective material by keeping the hands away from the nose and mouth by the routine sterilization of dishes and silverware and by the use of individual drinking glasses even within the family

AIR DISINFECTION AND DUST SUPPRESSION

Since respiratory infections seem to be trans mitted from person to person primarily through the air it is logical to assume that they could be prevented or substantially reduced if we could rid the air of disease producing or ganisms much as typhoid fever and other water borne diseases have been practically eliminated by the purification of drinking water

Dust suppression measures to reduce con tamination of the air we breath are feasible and recommended For the disinfection of air ultra violet radiation and germicidal vapors of hypochlorous acid or propylene and triethyl ene glycol are effective under experimental conditions They have not however reduced respiratory infections when utilized in schools factories or military barracks Practical meas ures in this area therefore remain for the future[30]

AVOIDANCE OF CHILLING

Those who are leading relatively sedentary indoor lives will have less colds if they avoid drafts and other kinds of exposure and chilling Adequate and proper clothing and shoes to keep the body warm and the feet warm and dry are important This is especially true with children Places of work and residences should be warm and free from drafts but not overheated

The ventilation of sleeping quarters should be regulated in accordance with outside at mospheric conditions keeping in mind the fact that drafts are undesirable and that sleep is most restful in an atmosphere which is cool rather than warm or cold

DIETARY MEASURES

Many dietary measures are recommended for the prevention of colds but none of these is based upon scientific evidence or established fact For the maintenance of health a com plete adequate and balanced diet is necessary but beyond this no special diet has been demonstrated to be of value for either the pre vention or the cure of colds

Among dietary factors the *vitamins* are ex tensively exploited for the prevention of colds Repeated studies have shown that both ani mals and man have a decreased resistance to infections of various kinds when suffering from vitamin deficiencies Apparently this may be true for each of the better known vitamins Most of the studies of vitamins for the preven tion of colds have been limited to vitamin A vitamin C or to vitamins A and D as contained in cod liver oil The experiments with vitamin A and C have resulted almost uniformly in negative results Cod liver oil has been re ported by a number of authors to reduce the severity and by some the frequency of colds

Most of these reports, however, are based upon inadequately controlled studies.

Investigations of the use of multiple vitamins for the prevention of colds have been few and inconclusive. Yet, if vitamins have any value, it should be demonstrable by administering adequate dosages of well selected vitamin mixtures. Such mixtures in a carefully controlled study were administered to University of Minnesota students during the school year 1940–41.[40] The only conclusion that can be drawn from this study is that large doses of vitamins A, B_1, B_2, C, D, and nicotinic acid have no demonstrable effect on the number or the severity of upper respiratory infections when administered to young adults who presumably are already on a reasonably adequate diet.

VACCINES

For a number of years my collaborators and I conducted carefully controlled studies concerning the value of various measures advocated for the prevention and treatment of colds. In these studies we included several bacterial vaccines. Two of these were administered hypodermically, two by mouth and two by spraying into the nose.

At the beginning of these studies students who volunteered to take the treatments were assigned alternately and without selection to control groups and to experimental groups. The students in the control groups were treated in exactly the same manner as those in the experimental groups but they received blanks instead of vaccine. All students thought that they were receiving vaccine and so had the same attitude toward the study. The students in all groups were instructed to report to the Health Service whenever a cold developed and to keep a record of each cold of more than 24 hours' duration. The physicians who saw these students at the Health Service had no information as to which group they represented.

Subcutaneous Administration

The students who received by injection the oldest and most widely used cold vaccine reported that during the previous year they had averaged 4.7 colds per person, but that during the year that they were taking the vaccine they averaged only 2.1 colds per person. This is a reduction of 55%, apparently an excellent result. In fact, it is just as great a reduction as has been reported in the studies which conclude that these vaccines are of value.

Unfortunately, so far as the hopeful side of this picture is concerned, we had a control group, which consisted of subjects who received injections that they thought were vaccine but were essentially nothing but sterile water. This control group reported that they had an average of 4.9 colds during the previous year and 1.9 colds during the year of the study, a reduction of 61%. In other words, this group which got nothing of any possible value for the prevention of colds reported just as good results as did the group which got the vaccine.[41]

Such results reported by a "control group" are exceedingly significant because they show how easily and unjustifiably enthusiastic one may become concerning any procedures or preparations, no matter how worthless, for prevention of colds when skilful advertising or well meaning but uncritical friends recommend them. Furthermore, how completely one can be misled or mistaken in judging the value of preparations for the prevention of colds was illustrated by telephone calls and letters received from physicians the winter following this study stating that individuals who *had been University students the year before* and had participated in our cold prevention studies had come to them asking for the same kind of vaccine that they had received at the University. Their reason for the request was that they had had three, four, or five severe colds every winter until last year when they took this vaccine and did not have a single cold. What could be more convincing except for the fact that the records showed that they were in the "control group" and that the injections they received *contained only sterile* water.

Oral Administration

Oral vaccines for colds consist of essentially the same organisms as are contained in the vaccines for subcutaneous use. They are

killed by heat and administered in capsules or tablets. In our study of this vaccine the students in the experimental group received capsules containing vaccine while the students in the control group received capsules filled only with sugar. These two types of capsules were indistinguishable and were prescribed with exactly the same instructions.

In this study the vaccinated group reported a reduction of approximately 70% in the average number of colds per person in the year of study as compared to the number of colds which these individuals said that they had had during the previous year. This is approximately the same reduction as has been reported by other investigators and looks like an excellent result. However, when we turn to the control group, we again find just as much reduction as was reported by the vaccinated group. During the year of the study the vaccinated group reported an average of 2.1 colds and the control group 2.0 colds per person. Also the time lost from school was exactly the same for the two groups.[42]

Similar conclusions concerning the worthlessness of cold vaccines are drawn by McGee, Andes, Plume and Hinton from a controlled study among industrial and office workers in five plants of the Hercules Powder Company. In these studies they administered two vaccines by injection and three by the oral route.[43]

Intranasal Administration

Still a third method of administering cold vaccines was studied. That was to spray the vaccine into the nose as advocated by Walsh. The rationale for this method of administration is the assumption that the application of the vaccine to the nasal mucous membranes stimulates the development of local tissue immunity as well as general immunity. Walsh has reported some hopeful preliminary results, but our studies fail to show any less colds in the vaccinated group than in the control group.[44]

Vaccines Against Other Acute Upper Respiratory Infections

A vaccine has been developed which is effective in preventing influenza caused by recognized and established strains of influenza virus.

There is some evidence also that it may be possible to prepare effective vaccines against some of the other upper respiratory viral infections such as those caused by the so-called adeno viruses.[4] These conditions, however, are distinct from the common cold and give no immunity to colds.

NASAL SPRAYS, MOUTH WASHES, GARGLES, AND ANTISEPTICS

Nasal sprays, mouth washes, gargles and antiseptics may destroy germs in test tubes if given sufficient time, but none of them acts instantaneously nor are they effective in the weak solutions which can be tolerated by the membranes of the nose and throat. Further, only a very small proportion of these membranes can possibly be reached by sprays, mouth washes, gargles or antiseptics.

TREATMENT OF COLDS

BED REST

It is frequently said that if you treat a cold you can cure it in 14 days, and if you do nothing about it you will be well in two weeks. And a favorite prescription is a couple of dozen soft linen handkerchiefs and 10 days in bed. Such skepticism as to the value of treatment of the common cold is amply justified by most experience.

First as to bed rest. "Go to bed when you have a cold and stay there until you are well" is good advice. Its value lies in protecting others from exposure, in increasing general resistance and in keeping the body warm. Bed rest during the acute stages of colds supplemented by such treatment as is indicated would doubtless diminish their severity, limit their spread and reduce the frequency of complications. Unfortunately, like most good advice, this rarely is followed. Most people just will not stay in bed unless they feel ill.

Most of these reports, however, are based upon inadequately controlled studies.

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HOT BATHS

Hot baths for the treatment of colds may consist of hot water, hot air, or steam The effect of these baths is to dilate the blood vessels of the skin and to increase blood flow through them As a result, nasal congestion and stuffiness are reduced

EXERCISE AND MASSAGE

Similar effects may be obtained with massage or other forms of physiotherapy, with hot or cold compresses, mustard plasters, and certain medicated ointments If such treatments are followed by rest in bed with sufficient covers to prevent cooling, the effect is prolonged and the possibility of their being of more than temporary benefit is increased

Exercise is frequently utilized by athletes for the treatment of colds They describe it as "sweating out" a cold What they experience is relief of nasal stuffiness, and possibly of discharge, as a result of the exercise This occurs, as with hot baths, because of the increased flow of blood to the muscles and the skin Such relief is only temporary, but occasionally it does seem to prevent further progress of the cold Usually, however, the symptoms recur when the body gets chilled and then the cold may become even more severe than before

LIQUIDS

Large quantities of liquids in the form of water, lemonade, orange juice, or other drinks have long been considered a valuable aid in the treatment of colds The purpose of these is to increase excretion, thereby presumably aiding in the elimination of the supposedly toxic products produced by the infection This sounds plausible, but actually the practice of forcing fluids for colds is based upon assumption rather than upon evidence of its value Some studies recently reported from the military services suggest that reduction of fluid intake to the minimum which the patient will tolerate decreases symptoms and accelerates recovery A small scale study of our own, however, revealed no difference in the length of hospitalization of university students with acute respiratory infections whether fluids were forced, restricted, or given ad lib

MEDICATIONS

The cold medication of greatest age is the old fashioned Dover's powder. This was first proposed by Thomas Dover in the latter part of the Seventeenth Century for the treatment of gout Originally it contained powdered opium, powdered ipecac, and potassium chlorate and was administered with a half pint of grog Some time later the potassium chlorate and the grog were omitted and the powder of opium and ipecac came to be used for colds This was probably because the preparation had obtained a reputation as a sweating powder and sweating was supposed to be beneficial

Approximately 25 years ago we made a chance observation that morphine seemed to give prompt and effective relief in several individuals with acute head colds This was merely individual experience, but the effect was so consistent that a study was undertaken to determine whether similar results would occur in other persons[48]

This study, which was carried out by the Students' Health Service of the University of Minnesota, was specifically planned to avoid prejudice for or against any particular medication To accomplish this the following procedure was adopted Physicians wrote prescriptions for "cold medication" These prescriptions were filled by a pharmacist who used in sequence the medications being studied at the time Neither physician nor patient knew what medication had been given After 48 hours of treatment the patients reported results on cards prepared for this purpose Upon the basis of these reports the effectiveness of the medication in each case was estimated Finally, the pharmacist's record was obtained and the results were tabulated according to the various medications which had been used

At the outset of the study some of the tablets and capsules given out contained only milk sugar These were included so that we might know what proportions of patients would recover without treatment in the 48-hour period

for which results were reported. In other words the group who received sugar tablets thinking that they contained medication served as a "control group" for the rest of the study. The importance of having this control is clearly shown by the results for approximately 35% of the students who got the sugar tablets reported definite improvement or "complete cure" of their colds within 48 hours. In fact some of them experienced such prompt and remarkable improvement that they were moved to comment that this medication was the most effective treatment that they had ever tried for their colds. Certain of the reports were so enthusiastic that they would serve as splendid testimonials as to the value of sugar tablets for the cure of colds.

The initial purpose of this study was to determine whether morphine is of value in the treatment of acute colds. It was not long before this question could be answered in the affirmative. Morphine however is obviously unsuitable for general use in the treatment of such a widespread condition as the common cold. Consequently the scope of the investigation was extended in the hope of finding some other preparation which would be effective without possessing the disadvantages of morphine.

Since morphine is obtained from opium we turned our attention to other derivatives of opium which are less toxic and carry no practical danger of habituation. Codeine and papaverine were the first two of these to be investigated. Both gave evidence of value in the treatment of acute colds but neither was so effective as morphine. Next because of the fact that codeine and papaverine are quite different chemically it was decided to try them in combination on the chance that they might be effective in different individuals.

Later other drugs which are extensively used for the treatment of colds were studied in order that their effectiveness might be evaluated in relation both to the control tablets and to the other drugs used. In order that the presentation of the results of these studies may not be too confusing I have arbitrarily divided the medications studied into three groups (1) those of greatest value (2) those of moderate value and (3) those of little or no value.

Medications of Greatest Value

The medications of greatest value according to these studies are all derivatives of opium. This is particularly interesting in view of statements that opium addicts rarely have colds. Concerning this Thomas De Quincey in his *Confessions of an Opium Eater*[47] wrote "It is remarkable that during the whole period of years through which I had taken opium I never once caught cold as the phrase is nor even the slightest cough. But after discontinuing the use of opium a violent cold attacked me and a cough soon after." In similar vein writes Cocteau in his *Diary of an Addict*[48] "Opium he says is a season. The smoker no longer suffers from changes in the weather. He never catches cold." And at another place "Without opium I am cold I catch cold I have no appetite. When smoking I am warm. I don't know what colds are. I am hungry. My impatience disappears."

Our studies indicate that *morphine* and *dilaudid* which is a derivative of morphine both give relief in about 75% of patients with acute head colds. However because of their toxicity and addictive possibilities neither of these drugs is suitable for general use.

The *codeine papaverine* mixture referred to was tried in different combinations proportions and dosages. Finally a preparation consisting of one quarter grain of codeine and one quarter grain of papaverine was selected as most suitable for this purpose. Of 1 500 students who were given this preparation for the treatment of acute head colds 72% reported definite improvement or complete relief within 24 to 48 hours. While taking this medication most of the students were up and about and attending classes. Had they remained in bed while using it it is possible that even better result might have been obtained. The earlier in the course of the cold that this preparation is used the larger the proportion of good results. In fact the most effective way to use it is to have it available to take it at the very onset of symptoms.

The usual dosage of this preparation commonly called "Copavin" for an adult is one tablet after each meal and two at bed time or one tablet every three hours and two at bed

time For best results, however, this dosage should be modified in relation to the severity of symptoms and the reaction of the patient to the medication For example, if symptoms are severe, two tablets instead of one are indicated for the first or the first and second doses and three instead of two may be given at bed time. The dosage for children should be regulated in relation to size If treatment is begun at the very beginning of symptoms, a few doses may be all that are required If the cold is well established, it may be necessary to continue the medication for two or three days

The chief beneficial effect experienced by those who use this preparation is a marked decrease or complete disappearance of nasal congestion and discharge In many cases with the relief of these symptoms the progress of the cold is arrested and the stage of protracted nasal discharge avoided

Since our original publication of these studies confirmatory reports have been published by several other investigators Doctor Russell Cecil of New York states that he "can highly recommend the prompt administration of the popular papaverine and codeine mixture when given at the first intimation of a cold When several of these capsules are taken *at the very beginning* of a cold, infection can frequently be aborted "[49]

Reporting on his experience with this medication Doctor Fritz Hutter of Vienna writes, "If my experiences differ from those of the initiator of the method, it is in the fact that the treatment has really not failed me, so far as I can survey my cases, a single time

Therapy was not attempted in patients with allergic rhinitis nor in the later stages of colds, when the nasal discharge had become thick and purulent To be effective this treatment must be begun in the early stages of acute coryza while the nasal discharge is still thin and watery At this stage a few doses may entirely abort the cold But if this does not occur, sufficiently early treatment definitely shortens the course of the disease and prevents or markedly diminishes the development of the thick, irritating nasal discharge with its attendant symptoms "[50]

Medications of Moderate Value

The medications of moderate value include *codeine* alone, *papaverine* alone, powdered *opium, Dover's powder,* and *quinine* The proportion of individuals who reported "complete relief" or "definite improvement" after the use of these preparations ranged from 57% for powdered opium down to 50 percent for quinine.

Medications of Little or No Value

Among the medications of little or no value are included the preparations from which less than 50% of subjects reported benefit In this group are *aspirin, calcium* and *iodine, halibut liver oil, amytal, ephedrine, atropine,* an *aspirin phenacetin caffein compound,* and *soda*

Although *aspirin* ranks at the top of this group, the results from it are but little better than from the sugar tablets

Space does not permit comment concerning the other medications which proved of little or no value, but, since one hears so much concerning alkalization in the treatment of colds, attention should be called to the fact that although soda was given in large dosages, the results were the same as those reported for the sugar tablets

Advertised Cold Remedies

Mention should be made also concerning the results obtained with two *nationally advertised medications* for the treatment of colds One of these is an internal medication which was purchased on the "open market," removed from the original containers and administered unlabeled to a series of students in this study The directions given with this medication were those recommended by the manufacturer The results were not significantly better than those obtained with the sugar tablets, 44% as compared to 35% reporting benefit Furthermore, 14% of the students who took this medicine reported unpleasant symptoms after its use

The other of these commercial preparations was the most extensively advertised and widely sold "nose drops" for the prevention and treatment of colds A supply of this was purchased at a local drug store This was transferred to unlabeled bottles and dispensed to students with the directions recommended by

the manufacturer. Thirty one per cent of the students who used this medication reported benefit from it, thereby putting it in the same class as sugar tablets so far as the effective treatment of colds is concerned.

This is just one of many advertised preparations to be dropped or sprayed into the nose for the prevention or cure of colds. People think that they are benefited by them because they give temporary relief of congestion and stuffiness. Little do they realize that medicated oily preparations in the nose, whether applied by spraying or dropping, interfere with the action of the cilia and may even destroy respiratory epithelium.[51] For this reason, as well as because of the irritation which many of these preparations produce, most nose and throat specialists advise against the introduction of medicinal preparations into the nose except when they are definitely indicated for the treatment of some specific condition.

Another objection to the use of such preparations is the danger of lipid pneumonia that may result from the inhalation of oily substances into the lungs. In reviewing this subject, Paul Cannon, Professor of Pathology at the University of Chicago, states:

"The intranasal use of medicated oils is widespread not only in medical practice but also in home medication. Although physicians are beginning to discourage the custom, many persons continue to use nasal oils because of the extensive advertising campaigns of the makers. One company over the radio urges everyone with symptoms of a beginning cold to put 'a few drops in each nostril when needed.' No warning is given as to the possible harm resulting from their excessive or habitual use. Abandonment of this type of medication will be slow because of the fact that so many persons use oily nose drops with no apparent ill effects. This, however, no more indicates the harmlessness of the practice than does the occasional ingestion of small amounts of lead prove that it is not poison and therefore can be eaten repeatedly over a long period."

Other Treatments

Of the other treatments suggested for colds alcohol is the most popular. Whiskey, brandy and "hot toddies" have long been recommended for the treatment of colds. Scientifically there is some basis or excuse for the use of alcohol in colds, namely, that alcohol causes an increase in the blood flow to the skin with a resultant feeling of warmth if one is wet and chilled. On the other hand, alcohol itself causes nasal congestion in some people and many reliable studies have shown that the continuous or excessive use of alcohol lowers resistance to pneumonia, the most serious complication of colds.

Cathartics

Cathartics of various kinds have long been a home remedy for colds and are included in many of the cold medicines advertised to the public. The reason for their use has been the assumption that catharsis aids in the elimination of the infection or of some poison thought to be present in colds. Logically there is no justification for any such belief, and two studies show that cathartics are of no value in colds and that patients who take them lose more time from work than those who do not.

Antihistamines

In a controlled study in which 980 colds were treated in 367 supposedly non allergic individuals we found no evidence that the antihistamines have any beneficial effect upon the duration or the severity of colds. Other well-controlled studies have led to similar conclusions.[54]

Sulfa Drugs

Sulfa drugs of various kinds have been promoted and by some physicians extensively prescribed for the treatment of colds. Some of these have been used locally in the form of nasal sprays, but most have been administered orally. This group of drugs is clearly of great value in the treatment of various streptococcal or other bacterial infections, including the complications of the common cold. On the other hand, there is no evidence that sulfonamides are helpful in the treatment of colds and there is a possibility that they may be harmful.

Antibiotics

Antibiotics also are widely prescribed for the treatment of colds sometimes singly and sometimes in various combinations There is, however, no evidence whatsoever that any of these are beneficial for the prevention or the treatment of viral, non bacterial respiratory infections[56] When children who have had rheumatic fever acquire acute respiratory infections, the administration of antibiotics or sulfonamides is recommended to prevent reactivation of the rheumatic fever It has been shown, also, that some long acting types of penicillin given at regular intervals throughout the year are useful in the prevention of recurrences of rheumatic fever Likewise, antibiotics are helpful in the treatment of certain complications of colds They should be administered, however, only when clearly indicated and then in adequate dosage to produce results The indiscriminate use of antibiotics in small dosages does no good and may sensitize patients to these valuable drugs so that they cannot be used when urgently needed Furthermore, such usage may result in the development of strains of the infectious organisms which are resistant to these antibiotics

Ascorbic Acid and Bioflavonoids

Extensive promotion has recently been given to the presumed value of ascorbic acid and bioflavonoids in the prevention and treatment of colds Several controlled studies, however, show no value from 1 gm of bioflavonoid and/or 200 mg of ascorbic acid administered daily in aborting or curing the common cold

SUMMARY

Finally, a brief summary of our present knowledge concerning the prevention and treatment of colds

(1) There is no measure that is specific or uniformly effective for the prevention of the common cold or of other respiratory infections[58]

(2) General measures of value in increasing resistance are adequate rest, exercise and baths, to keep the circulation in good tone, a diet that is adequate and well-balanced, moderate in quantity and containing liberal amounts of fruits and vegetables

(3) Important among the more definitive preventive measures are adequate clothing and proper ventilation to avoid chilling, the avoidance of exposure both direct and indirect, to persons who have colds, the recognition diagnosis, and correction of allergic conditions and the removal of obstructing or definitely diseased tonsils and adenoids

(4) Vitamin supplements to adequate well balanced diets have not been shown to increase resistance to colds However, if diets are limited, the use of dietary supplements may be advisable for their general health value

(5) Vaccines have not been shown by critical studies to be of sufficient value to justify their widespread or indiscriminate use, although their use may be justifiable in occasional, carefully selected individual cases

(6) There is no specific cure for the common cold

(7) Bed rest during the early stage of a cold is advisable, and, if the cold is accompanied by fever or general aching, it is essential

(8) Hot baths, counter irritation and exercise give temporary relief of nasal stuffiness and discharge by increasing blood flow to the muscles and skin Exercise when one has a cold, however, is unwise because of the danger of complications

(9) A critical study of medicinal preparations for the treatment of colds shows that the best results are obtained with derivatives of opium Of these most effective and suitable for general use is a mixture of codeine and papaverine If administered at the very beginning of symptoms, approximately 75% of patients with acute head colds experience 'complete relief" or "definite improvement' within 24 to 48 hours

(10) In subacute and chronic colds and in acute pharyngitis none of the preparations studied seemed to influence the course of the infection, although some give symptomatic relief

(11) Nasal drops and sprays may afford temporary relief of nasal stuffiness but involve the hazard of chronic irritation and lipid pneumonia

(12) The sulfa drugs and antibiotics are of no value in the treatment of colds although they may be useful in certain complications of colds

(13) The public wastes millions of dollars annually for cleverly advertised but completely worthless cold medications Many of these are harmless, but some are prejudicial to health

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CHAPTER 5

Pertussis (Whooping Cough)

William L Bradford, M D

DEFINITION

Pertussis is an acute infection of the respiratory tract caused by *Hemophilus pertussis* It is characterized by a spasmodic cough, often strangling in nature, which frequently but not always terminates in a forceful inspiration (the whoop) and in vomiting

HISTORY

The earliest reference to the disease appears to have been made by Moulton near the middle of the Sixteenth Century De Baillou however, is credited with the first classical description in 1578

Our modern knowledge began in 1906 when Bordet and Gengou discovered the causative organism Mallory (1913) described the pathological lesions and described attempts to reproduce the disease experimentally Smith (1927) and Gallavan and Goodpasture (1937) made significant contributions to our knowledge of the pathology of the disease

The classical cough plate method for the bacteriological diagnosis of pertussis was introduced by Chievitz and Meyer (1916) and the nasopharyngeal swab method was described by Bradford and Slavin (1940) Madsen (1925) and Lawson (1927) made important bacteriological contributions

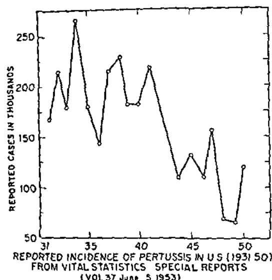
In 1933 the disease was produced experimentally in susceptible children by MacDonald and MacDonald with a culture of H pertussis In a similar manner, it was successfully reproduced in the chimpanzee by Shibley and Hoelscher (1934) Experimental infections have also been produced in the puppy, the monkey, the mouse and the rat

Important contributions towards the development of effective methods of active immunization were made by Leslie and Gardner (1931), Madsen (1933), Sauer (1939), Kendrick and Eldering (1936), Faber and Miller (1940) and others

Recent studies on the antigenic structure of H pertussis by Mishulow (1930), Evans (1940), Flosdorf (1940), Miller (1934), Strean (1940) have added much to our immunological information In recent years, the possible role of hypersensitivity in pertussis has been stressed by Toomey, Parfentjev, Pittman and Bradford

INCIDENCE

Whooping cough is encountered sporadically and endemically throughout the world Epidemics occur irregularly at intervals of from two to four years in our more thickly populated areas Since 1935 there has been a decided decrease in the incidence of the disease



REPORTED INCIDENCE OF PERTUSSIS IN U S (1931 50) FROM VITAL STATISTICS SPECIAL REPORTS (VOL 37 June 5 1953)

as shown in Figure 1 The majority of cases occur during winter and spring but the disease is common during the summer months In certain communities its seasonal incidence more nearly resembles that of the diarrheal diseases rather than that of the respiratory infections In the South the peak of its incidence is in May, in the North in January or February Pertussis is more frequent among females particularly in the older age groups It is distinctly a disease of early life about 85% of the cases occurring in individuals under 7 years of age Infants under 6 months of age are especially susceptible and among them the disease exacts a high mortality The communicability rate is high both in family and in school room exposures In family exposures it is between 75 to 90% closely approximating that of measles and chicken pox

ETIOLOGY

Hemophilus pertussis discovered by Bordet and Gengou in 1906 is now regarded as the sole cause of the disease It is a minute Gram negative coccoid bacillus about 1 5 microns in length It occurs in great numbers upon the surface of the epithelial cells lining the upper respiratory tract during the catarrhal period of the disease In infants it can often be isolated in pure culture from the lungs at post mortem

IMMUNITY

Permanent immunity usually follows an attack of whooping cough though second attacks may sometimes occur It is highly probable that resistance to infection with H pertussis is both humoral and cellular but the relative importance of the two types of immunity is not known During the course of active infection or following injections of vaccine humoral antibodies appear and remain for a period of a few months

Recent studies indicate that the antigenic structure of the organism consists of at least three components the agglutinogen a heat labile toxin and a heat stabile toxin Both the agglutinogen and labile toxin seem to be of clinical importance the former being associated with antibacterial immunity the latter with antitoxic immunity The relative importance of antibacterial and antitoxic immunity is unknown but most investigators at the present time believe that antibacterial immunity is the more important

Attempts have been made to use the agglutinogen and the heat labile toxin as skin testing materials to determine susceptibility to the disease The value of neither is conclusively proved but it is of interest that a positive reaction with the agglutinogen suggests immunity while a positive reaction with the toxin suggests *susceptibility*

Active immunity against the disease can be induced by the injection of vaccine The vaccine however must be prepared from an anti*genic strain of the organism*

Passive protection may be given to the exposed infant by injection of hyperimmune human serum gamma globulin prepared from

it or immune rabbit serum Gamma globulin (Hypertussis) is the one generally used

The newly born infant receives practically no immunity from the mother but passive antibodies may be supplied by actively immunizing the mother during the third trimester of pregnancy—obviously not a practical procedure

PATHOLOGY

Catarrhal inflammation and a certain degree of hyperplasia of the epithelium in the upper respiratory tract is always present Upon the surface of the epithelial cells among the cilia and between these cells clumps of the minute organisms may be demonstrated by proper staining methods Purulent exudate and an excess of mucus accumulates in the lumina of the smaller bronchi and bronchioles A characteristic necrosis of the epithelium occurs As described by Gallavan and Goodpasture this occurs usually in the midzonal and basilar portions of the bronchial epithelium In these areas many polymorphonuclear leucocytes accumulate Peribronchiolitis is common extending from the hilum outward along the bronchial vascular rays to the middle or outer portions of the lungs

Typical interstitial changes characterized by infiltrations of large mononuclear cells and thickening of the alveolar walls follow The cellular infiltration is most marked around the bronchi These changes are more frequent near the hilum but often extend in a fan shaped manner toward the inner basilar areas of the lungs Hemorrhages and edema occur as early parenchymal changes In certain instances nuclear inclusion bodies may be found in the bronchial epithelium and in the large mononuclear cells a finding interpreted by certain workers as evidence of a viral etiological factor

The tracheobronchial glands are usually enlarged during the active and early convalescent stages of the disease This enlargement is chiefly caused by hyperplasia of the follicles of the glands and is the cause of the characteristic hilar lesion commonly observed by the x ray film

It is probable that H pertussis is responsible to a considerable degree for the major part of the lung lesion Superimposed upon this lesion however a variety of changes may occur produced by secondary invading organisms such as the *Hemophilus influenzae* *Staphylococcus* *Hemolytic streptococcus* and the *Pneumococcus* Minute abscesses purulent bronchitis and even typical lobar pneumonia may occur Well defined bronchiectasis may develop early in the course of the disease but it is more common as a sequelae In such cases one may note a change from the columnar to the squamous cell type in the bronchial epithelium along with fibrous organization of the tissues of the lung Emphysema is almost always present the presence of surface blebs on the lung being observed in practically all fatal cases

The changes in the brain observed by various authors have been described as circulatory degenerative and inflammatory Hemorrhages vascular spasms and edema have been described Various types of degenerative lesions in various parts of the brain have been observed Among the inflammatory lesions meningitis and encephalitis are the most important According to Dolgopol the changes are apparently non infectious and are most likely of circulatory origin consisting of edema ischemic cellular degeneration small multiple hemorrhages and lymphocytic plugs in the capillaries and veins She prefers the term Pertussis encephalopathy originally suggested by Jochims as the best designation for the brain lesions occurring during the course of the disease

CLINICAL MANIFESTATIONS

INCUBATION PERIOD

The incubation period is 10 to 14 days The mean duration of the period is 13 days according to Lawson

CLINICAL COURSE

The clinical course is roughly 6 weeks consisting of three stages the catarrhal paroxysmal and convalescent each lasting approximately 2 weeks Spasmodic coughing may occur for several weeks or months longer but there is little evidence that the causative organism remains in the respiratory tract beyond the sixth week

Catarrhal Period

The onset is usually insidious as a mild nocturnal cough which soon becomes diurnal as well It may resemble the common cold Sneezing is a common symptom The appetite fails The cough later suggests bronchitis and because of its persistence the physician is usually consulted Hoarseness may occur rarely the onset resembles that of acute obstructive laryngitis As the cough increases in severity suffusion of the conjunctivae with edema of the lower eyelids may be observed

Spasmodic Period

Near the end of the second week the cough is definitely spasmodic occurring in series of explosive efforts There may be forty to fifty violent expiratory coughs before the patient is able to inhale a full breath When he does inhale through the markedly spastic larynx a loud crowing stridor results the whoop During the paroxysm the child may grasp a nearby object for support the face becomes extremely congested often cyanotic and he may become markedly exhausted often mentally confused The veins of the neck and forehead are conspicuous and beads of perspiration may appear upon the forehead face or neck Small infants often become so exhausted and blue from the long period of apnea that artificial respiration or oxygen inhalation becomes necessary In such cases convulsions are common

Convalescent Period

After the fourth week of coughing the paroxysms diminish in frequency and severity but may continue for several weeks The appetite improves which is one of the first signs of recovery During an intercurrent infection such as a cold, the symptoms may reappear even to the extent of resembling a new attack

Pertussis is a variable disease often occurring in an extremely mild or atypical form It may last but a few days without definite paroxysms whoop or vomiting In infants the characteristic whoop may not occur but choking cyanotic attacks are common

COMPLICATIONS

PULMONARY

ne most important complication is bronchopneumonia This is usually interstitial in type Confluent bronchopneumonia ...ely lobar ...curs frequently and is often erroneously ...agnosed lobar from the roentgenogram Atelectasis is common and is likewise frequently interpreted as pneumonia It is caused by the temporary plugging of a bronchus by mucus Emphysema either vesicular or interstitial occurs in practically all severe cases Subcutaneous emphysema occasionally occurs when air from ruptured surface blebs escapes by way of the mediastinum into the tissues of the neck and chest Such cases are usually fatal In one observed by the author the total white blood cell count reached 257 000 Pneumothorax occasionally occurs empyema is rare

Pulmonary fibrosis and bronchiectasis are not unusual complications Bronchial asthma often begins within a year following an attack of pertussis The disease may cause a spread of an existing tuberculous lesion

That serious cardiac complications are associated with whooping cough is denied by some authorities although it seems certain that dilatation of the right side of the heart occurs in certain cases It is usually associated with a diffuse pneumonic process

OTITIS MEDIA

Otitis media occurs in about 10% of hospital cases *It is usually caused by secondary* invading organisms Smith records a case in which H pertussis was the *only organism iso*lated from the infected middle ear

CENTRAL NERVOUS SYSTEM

Convulsions occur in approximately 8% of hospital cases and are most common in infants The spinal fluid in such cases is usually normal Encephalitis has been described Epilepsy mental retardation and visual defects occasionally occur Temporary paresis of an extremity is a rare complication

HEMORRHAGES

Hemorrhages in the conjunctivae and epistaxis are frequent Blood tinged *sputum re*sults from small erosive lesions in the tracheal epithelium occurring during a paroxysm Hemorrhages of the brain have been described

Ulcer of the lingual frenum intussusception hernia and rectal prolapse are usually mechanical in origin

NUTRITIONAL

Dietary deficiencies resulting from pro*longed nutritional disturbances may occur* Rickets and scurvy are the most common ones observed

Purpura and leukemia have been reported as occurring during convalescence in a few instances

RELATIONSHIP OF SYMPTOMS TO PATHOLOGY

The initial lesion is caused by infection of the respiratory epithelium with H pertussis and the effect of its toxin The cough and the vomiting is probably reflex in origin and the characteristic whoop is produced by forceful inhalation through a spastic larynx Enlargement of the tracheal bronchial glands no doubt is a factor in exciting the cough reflex

The pneumonic lesion is primarily caused by *H pertussis and secondary invading organ*isms There is evidence that the lymphocytosis is caused by the action of the toxin of the organism on the hematopoietic system

Atelectasis results from obstruction of the air passages by mucus plugs This along with pneumonia and a volitional restriction of free breathing (for fear of exciting a paroxysm) prevents proper oxygenation of the blood This according to Regan and *Tolstoouhov* leads to a state of uncompensated acidosis Enlargement of the right side of the heart results from increased impediment of the pulmonary circulation

Anoxemia is said to be the chief cause of convulsions Edema of the brain hemorrhage specific toxin rachitic tetany and encephalitis no doubt explain their occurrence in certain cases Gastric tetany caused by alkalosis resulting from excessive vomiting has been reported No doubt convulsions associated with *ordinary hyperthermia occur*

Various types of hemorrhage hernia and rectal prolapse are the result of mechanical strain associated with coughing Ulcer of the lingual frenum results from continued forceful protrusion of the tongue over the edges of the lower incisor teeth during coughing

Loss of appetite vomiting and diarrhea cause weight loss The resulting state of im*paired nutrition if not* corrected makes the subject exceedingly vulnerable to attack by all manner of secondary infections

DIAGNOSIS

Whooping cough should be suspected when a spasmodic cough persists of which examination reveals no other apparent cause In mild atypical cases and in the early stage of the disease bacteriological aid is necessary for accurate diagnosis A history of definite ex*posure obviously helps* It may be necessary to observe the progress of the cough for a few days An inquiry concerning previous active immunization should be made because a modi

fied type of the disease may be expected when vaccination fails to completely protect.

Certain other diseases produce symptoms which may be mistaken for those of pertussis. Persistent spasmodic cough may be caused by infection of the adenoids or nasal sinuses, allergic reactions, infection of the trachea with *Hemophilus influenzae* and even with *Brucella bronchiseptica*. Parapertussis resembles mild pertussis and can only be differentiated by culture. The author has observed cases of atypical pneumonia in which the coughing closely resembled that of whooping cough. The cough of early measles may be mistaken for pertussis but the occurrence of Koplik's spots and the exanthem should soon leave little doubt concerning the diagnosis.

The most helpful laboratory test is isolation of the organism from the upper respiratory tract. This may be done by the cough plate or the nasal swab culture methods. During the catarrhal period positive cultures may be expected in from 70 to 90% of the cases. A single negative culture does not rule out the disease.

During the late catarrhal or early paroxysmal stage a progressive increase in the total white blood cell count usually occurs. These cells may increase to 15 000 or 45 000 per cu mm of blood and show a corresponding increase in the absolute number of lymphocytes. In certain instances, usually complicated by pneumonia, extreme degrees of hyperlymphocytosis exist. Failure to observe the characteristic changes in the blood count does not rule out the disease.

Specific humoral antibodies appear during the third and fourth weeks of the disease. In certain instances diagnosis may be suggested by their demonstration but obviously their late appearance reduces the general value of the procedure as a diagnostic aid. Tests for the presence of agglutinins, complement fixing and mouse protective antibodies are usually performed.

Recent attempts to employ the purified agglutinogen and the heat labile toxin of H pertussis as materials for skin tests to determine susceptibility have been made. The results, though promising, have not fully proved their value for this purpose.

PROGNOSIS

The mortality rate of pertussis, like that of other communicable diseases, has greatly decreased during the past three decades. In the United States the total number of deaths and the death rate per 100 000 population for the years 1949–1953 were as follows:

Year	Number Deaths	Rate
1949	727	0.5
1950	1116	0.7
1951	951	0.6
1952	402	0.3
1953	270	0.2

However, among infants the disease remains one of the most fatal of the ordinary contagious group.

The percentage of distribution of ages of patients dying of pertussis in 1953 was:

Age	Per Cent
Under 1 year	68.5
1 year	15.0
2 years	6.3
3–4 years	4.0
5–9 years	3.1
Over 10 years	2.9

The disease is decidedly more fatal in rural areas.

PREVENTION

The young infant should be carefully protected from exposure. He should receive passive immunization. Complete protection or modification of the disease in exposed in

fants may be conferred by intramuscular injection of *10 to 30 ml* of hyperimmune human serum of 2 to 5 ml of gamma globulin prepared for it or 5 to 10 ml of immune rabbit serum

Active immunization should be routinely carried out at the third month of age or earlier by the intramuscular injection of a suitable vaccine This vaccine is usually combined with diphtheria and tetanus toxoid

A total of 12 antigenic units should be given in divided doses The antigenic potency of this amount must be derived from not more than 96 billion organisms in a liquid preparation or from not more than 48 billion organisms in a precipitated preparation

Booster injections of 3 units should be given at 1 3 and 5 years after the original course and at the time of an exposure Vaccines containing 4 antigenic units per 0 5 cc are available

TREATMENT

General symptomatic care is important The patient should be kept in a quiet environment *at a temperature of 65 to 75°F When vomiting occurs frequent small feedings* are better than fewer large ones

P R #206805 male aged 6 weeks Admitted 7 1-43 In third week of whooping cough Source of infection 3 siblings Rapid respirations substernal retraction cyanosis and convulsions Wbc 157 000 80% Lymphocytes Cultures and mouse inoculations of material from the nose and throat revealed no pathogenic organisms No response to therapy Died 8 hours after admission *Anatomical Diagnosis (A 7982)* tracheitis bronchitis interstitial broncho pneumonia small pulmonary hemorrhages Cultures from the lung at *post mortem revealed a pure growth of H* pertussis No secondary invading organisms isolated

TABLE I

RELATIONSHIP OF POSITIVE SKIN TESTS (AGGLUTINOGEN) TO THE HUMORAL AGGLUTIN TITER IN A GROUP OF VACCINATED CHILDREN

Agglutinin Titer	*Total Number*	*Actual Number*	*Expected* Number*
0	15	9	10
10–160	57	43	45
320	27	26	27

Titer	*Escaped Infection*
0	66%
10 160	79%
320	100%

* Sako found the following percentage of vaccinated children escaped the disease in family exposures according to their agglutinin titer

While the results obtained with the toxin have been disappointing there appears to be in general good correlation between the reaction obtained with agglutinogen and humoral antibodies (Table I)

In one of our studies we found the correlation *between the number of positive reactions* and the expected number of immune subjects fairly good

The severely ill patient should receive hospital care Oxygen therapy is indicated when cyanosis of vonculsions occur, or even when *the respiratory rate is rapid* A trained nursing personnel is exceedingly important X rays of the lungs and a tuberculin test should be made during convalescence

SPECIFIC

Vaccines possess little or no value unless given early in the disease to one previously immunized with vaccine

Serums There is evidence that gamma globulin prepared for hyperimmune human serum (Hypertussis Cutter) given in 2 5 cc amounts intramuscularly every other day for three injections is effective

Chemotherapy The broad spectrum antibodies aureomycin *terramycin and chloram*phenicol appear to be of about equal value Each of these drugs when given in a dosage of *50 mg per kilogram per day* is usually effective There is no advantage to be gained by giving a combination of them None is specific

SUMMARY

Pertussis is a disease of the entire respiratory tract. Because of its frequent harmful effect on the lungs, it deserves important consideration.

Since the discovery of the causative organism in 1906 important advances have been made in clinical and immunological studies of the disease. More exact knowledge of epidemiological factors, improved methods of bacteriological diagnosis, and more detailed information concerning the antigenic structure of the organism has resulted.

Recent successful attempts to reproduce the infection experimentally have afforded a more complete knowledge of pathology and have made possible the testing of certain therapeutic agents.

The important complications involve the pulmonary and central nervous systems. Broncho pneumonia, bronchiectasis, chronic fibrosis, emphysema and atelectasis are the most common pulmonary complications. Convulsions, encephalitis, and mental changes may result from involvement of the central nervous system.

Passive and active methods of prevention are effective. Modification of the disease when complete prevention fails is one of the important results of such procedures.

Treatment of severely ill infants is best carried out in a hospital. Expert nursing care is essential. A combination of chemotherapy and antiserum (Hyperimmune human or immune globulin) constitutes an effective therapeutic measure.

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CHAPTER 6

Diagnosis and Treatment of Diseases of the Trachea and Bronchi

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KNOWLEDGE of the anatomic structure of the airway is of great value in the diagnosis and treatment of diseases of the trachea and bronchi. A detailed description of the segmental anatomy of the lung will be found in another chapter of this book written by Boyden. The tracheobronchial tree is not a static structure; it elongates and expands during inspiration and shortens and contracts during expiration. This action often plays an important role in the variations of the physical findings and clinical symptoms in tracheobronchial disease.

ANOMALIES OF THE TRACHEOBRONCHIAL TREE

Congenital anomalies of the tracheobronchial tree are relatively rare. It is remarkable how seldom even minor deviations from the normal bronchial pattern occur in the human being. On extremely rare occasions the ventral bud of the primitive pharynx may fail to develop, resulting in agenesis of the lung. Improper development of the ventral bud may produce lobar agenesis. It is also possible to have aplasia of the lung with the appearance of a rudimentary bronchus but with elaboration of an alveolar parenchyma. In hypoplasia such rudimentary bronchi are associated with meager alveolar distribution in the whole or in part of the lung.

A bronchus occasionally may arise from an abnormal position; if this abnormality is not recognized, it may lead to considerable confusion and even to serious consequences if surgical procedures are attempted. Such an abnormality is illustrated in Figure 1. In this case the left main bronchus terminated in a blind pouch approximately 2.5 cm. from the bifurcation of the trachea, and the bronchus that supplied the left lung originated from the medial wall of the right main bronchus 1 cm. below the carina tracheae. Similar bronchial openings at times may originate from the trachea or from the bronchi that supply aberrant lung tissue (Fig. 2). It is important that such abnormal bronchi be recognized because this aberrant tissue may become involved in such diseases as tuberculosis, carcinoma and abscess, and if not properly localized may offer considerable difficulty from the standpoint of treatment.

An unusual anomaly is a tracheal diverticulum, which usually originates in the lower portion of the trachea on the right side. The walls of the diverticulum usually have the same structure as the trachea itself and are covered with normal mucous membrane. According to Chiari, such an anomaly represents the incompletely developed offshoot of a third bronchus originating about the bifurcation. When multiple diverticula of the trachea are present, the condition frequently has been termed "tracheiectasis" or more properly "tra-



Fig. 1. Abnormality in which the left main bronchus ends in a blind pouch and the left main bronchus originates from the right main bronchus



Fig. 2. Anomalous bronchus arising from the trachea and passing to the right upper lobe

cheoectasis. On rare occasions tracheoectasis has been associated with a tracheocele. However a tracheocele may occur without tracheoectasis. Bronchial diverticula situated on the mesial wall of the stem bronchi between the bronchi to the upper and middle lobes have been described. Congenital cysts arising in the wall of the trachea also are encountered occasionally.

ACUTE LARYNGOTRACHEOBRONCHITIS

Acute laryngotracheobronchitis is an intense inflammation of the larynx, trachea and major bronchi commonly occurring in children. It may start with coryza as in a common cold but is soon followed by hoarseness, croupy cough, stridor and dyspnea. When respiration is difficult cyanosis may ensue. The child frequently is severely ill and may be struggling to breathe but the degree of fever is not related to the severity of the disease. The mucous membranes are red, swollen and edematous and they may obstruct mechanically the passage of air in the glottis or the subglottic region. Thick and sticky secretions may also play a role in respiratory obstruction.

Bacteriologic examination of pharyngeal or tracheal secretions frequently reveals Micrococcus pyogenes, Diplococcus pneumoniae or Hemophilus influenzae but the etiologic agent in most cases is probably a virus with these organisms as secondary invaders. Bacteriologic studies can help differentiate this condition from diphtheria (Corynebacterium diphtheriae) and whooping cough (H. pertussis). Exposure to smoke and flame, nitrogen mustard gas or the smoke of white phosphorus is capable of producing a similar clinical picture.

Treatment should be directed primarily toward maintenance or restoration of an adequate airway. Immediate bronchoscopy followed by tracheotomy may be necessary and

lifesaving Occasionally the role of the bronchoscopist is merely that of being prepared to insert the bronchoscope if total obstruction should develop while tracheotomy is being performed When the condition is less severe it is reasonable to defer these procedures and observe the child closely while administering cool moist air or oxygen Moisture is most effectively added by aerosolized water detergent solutions or antibiotics such as penicillin Sometimes the addition of small doses of isopropylarterenol (isuprel hydrochloride) or epinephrine to the aerosolized solution reduces the laryngeal and tracheal edema sufficiently to improve the passage of air Parenteral use of antibiotics also is advisable

After an adequate airway has been established the prognosis is favorable Until then however, the outcome is uncertain and the prognosis is grave

VASCULAR DEFECTS

Alterations in the tracheobronchial tree may be produced by vascular abnormalities and diseases which may be either intrinsic or extrinsic in origin

Intrinsic vascular lesions are comparatively rare and consist mainly of hemangiomas and small aneurysms involving the small bronchial vessels Such lesions if of appreciable size and situated in the trachea or the main stem bronchi can be seen readily on bronchoscopic examination and treated adequately by bronchoscopic means Bleeding is usually the most likely symptom produced by such a lesion although lesions of considerable size occasionally may give rise to bronchial obstruction

Extrinsic vascular lesions are much commoner and may be divided into two main types namely (1) those resulting from developmental anomalies and (2) those due to organic changes involving the vascular system

DEVELOPMENTAL ANOMALIES

Developmental lesions may be of a great many varieties Symptoms if present usually occur early in life The diagnosis of vascular anomalies that may produce clinical symptoms can be made readily in most cases from the history and the roentgenologic examination Roentgenoscopic studies while the patient swallows barium are of tremendous value in the diagnosis of such lesions In addition useful information often is obtained on bronchoscopic as well as esophagoscopic examination Angiocardiography occasionally may be necessary to determine the nature of the lesion

Right sided Aorta

Among the commoner developmental anomalies that may produce tracheobronchial symptoms is a right sided aorta (Fig 3) Normally the aorta arises from the persistence and development of the left fourth branchial arch However should the aorta arise from the right fourth arch the result is a right sided vessel The right aortic arch may follow one of two



Fig 3 Right sided aorta which produced deformity of esophagus and partial compression of trachea



Fig 4 Esophagram in a case of double aortic arch

courses it may arch over the right primary bronchus and descend behind the lung and to the right of the esophagus in which case it is usually designated as an anterior right sided arch or it may pass backward and then to the left and behind the esophagus in which case it is designated as a posterior type of right sided aortic arch In the latter type great variations may occur in the branches that come off the aortic arch The major arch alone may pass behind the esophagus or there may be in addition a retro esophageal left subclavian artery that impinges on the esophagus at a higher level In some instances the left common carotid artery arises on the right from the proximal arch and extends across the arch and in front of the trachea producing compression of the anterior wall of the trachea and symptoms of obstruction

Persistent Double Aortic Arch

In those rare cases in which both the right and left aortic arches persist the anomaly may give rise to clinical symptoms As a rule the left arch is prone to pass anterior to the trachea and is usually smaller (Fig 4) In most instances both the trachea and the esophagus will be enclosed between the two branches of the aorta but on rare occasions only the trachea may be enclosed Although the space between the two branches of the aortic arch sometimes is sufficient to accommodate both the trachea and the esophagus without the production of symptoms it is much more likely that the space will not be adequate and either the trachea or the bronchus may be compressed When this occurs stridor cyanosis and choking spells are frequent If the esophagus is also involved dysphagia and regurgitation often occur The symptoms usually manifest themselves early in life and the infant has difficulty in breathing during the nursing period The degree of compression may be so great as to result in death unless the condition is recognized at an early stage and adequate surgical measures are instituted

Right Subclavian Artery

One of the commonest of the vascular anomalies that may cause tracheobronchial symptoms is a right subclavian artery that originates as the last left sided branch from the distal part of the aortic arch Such an anomalous right subclavian artery usually passes to its normal position by coursing from the left to the right side in front of the trachea or between the trachea and the esophagus or behind the esophagus crossing the midline of the trunk at the level of the third thoracic vertebra In cases of this kind the symptoms are more likely to be esophageal than tracheal in nature and the primary symptom frequently is transitory dysphagia which often has been termed dysphagia lusoria" As a rule dysphagia lusoria is more prone to occur after the second decade of life than earlier

ORGANIC CHANGES IN THE VASCULAR SYSTEM

An enlarged heart may impinge on the esophagus and cause symptoms but it is comparatively rare for such a lesion to involve the trachea Although enlargement of the heart may lead to displacement of the bronchus it is unusual for this to produce bronchial symptoms Dilatation of the left ventricle as in mitral stenosis may give rise to



Fig 5 Aneurysm of the aorta invading the left main bronchus

bronchial obstruction which always involves the left main stem bronchus

A much commoner cause of tracheobronchial difficulty is impingement on the trachea and bronchus by an aortic aneurysm (Fig 5) An aneurysm of the aorta not only may press on the bronchus, producing bronchial obstruction, but it may invade the wall of the bronchus and protrude into the bronchial lumen, causing obstruction and a clinical picture closely simulating that of tumor of the bronchus The development of an aortic aneurysm with impingement on the trachea or bronchus may be extremely slow or comparatively rapid The degree of bronchial obstruction may be pronounced

Bleeding is rather common in cases of aortic aneurysm in which the lumen of the trachea or bronchus is invaded The bleeding may be intermittent, although it is much more prone to be massive and fatal

In addition to involvement of the bronchus or trachea, an aortic aneurysm may impinge on the esophagus and produce esophageal obstruction or invade the esophagus with perforation into the esophagus itself

The diagnosis of aortic aneurysm may offer some difficulty, especially if the aneurysm occurs in a younger person and is not associated with positive results of serologic tests for syphilis In cases of this type roentgenologic examination of the thorax may be confusing because the findings are compatible with those seen in bronchial tumor Bronchoscopy may be of great value in the diagnosis, but care must be exercised in the removal of tissue from such a lesion for microscopic diagnosis because it may cause fatal massive bleeding It is important, in cases in which aortic aneurysm is suspected, that the patient have the benefit of a thorough clinical and fluoroscopic examination before any tissue is removed for microscopic study

TUMORS OF THE TRACHEA

Tracheal tumors are comparatively rare Because of the dramatic symptoms that tumors of the trachea may produce, they are always of special interest They may result from a great variety of causes but for purposes of discussion they are best divided into two categories namely malignant and benign Of 82 proved tracheal tumors studied at the Mayo Clinic, 47 were malignant and 35 were benign (see Table I)

TABLE I

CLASSIFICATION OF 82 PRIMARY NEOPLASMS OF THE TRACHEA

Malignant	
Squamous cell carcinoma	19
Cylindroma (adenoma)	18
Hemangio endothelioma	3
Myxofibrochondro osteogenic sarcoma	1
Adenocarcinoma	6
	47
Benign	
Papilloma	22
Tracheopathia osteoplastica	8
Amyloid tumor	2
Xanthoma	2
Chondroma	1
	35

MALIGNANT TUMORS

Although no portion of the trachea is immune to carcinoma, it occurs more frequently

in the lower half than in the upper portion It arises more frequently from the lateral and posterior wall of the trachea but occasionally may completely encircle the lumen It occurs more frequently in men than in women in a ratio of approximately 4 1 Although it may occur at any period of life it is most often seen in the later decades of life like carcinoma elsewhere in the body

Malignant tumors of the trachea may attain considerable size before giving rise to symptoms or the symptoms if present may be of such indefinite character that they may be easily disregarded Dyspnea stridor cough and less often hemoptysis and hoarseness are the symptoms most frequently encountered The patient's symptoms sometimes are misinterpreted as being due to asthma and this well exemplifies the old aphorism of Jackson that "all that wheezes is not asthma"

Although the diagnosis of a tracheal tumor often can be suspected or established by roentgenograms of the thorax or by tomography it is dependent in most cases on bronchoscopic examination The bronchoscopic appearance of the lesion is variable depending largely on the type of the malignant tumor As in primary carcinoma of the bronchus the exact diagnosis is dependent on the microscopic appearance of cells found in the secretion or of tissue removed from the tumor

Squamous cell carcinoma is by far the commonest malignant tumor of the trachea Adenocarcinomas are encountered less frequently and it is possible that these all originate primarily in a main stem bronchus and extend into and involve the lower end of the trachea

Adenoma of the trachea occurs with a frequency almost equal to that of squamous cell carcinoma Morphologically the adenomas in our series were all of the cylindroma type They may show evidence of peritracheal extension and may invade contiguous structures Widespread metastasis is rare

BENIGN TUMORS

Benign tumors of the tracheobronchial tree are comparatively rare They may produce the same symptoms that occur with malignant lesions involving the trachea As seen in Table I a variety of benign tumors may originate in the trachea



Fig 6 Calcified deposits in trachea in a case of tracheopathia osteoplastica Inset shows bronchoscopic appearance of the bony nodules in the trachea

Papilloma

This is by far the commonest benign tracheal tumor It originates from the surface epithelium and may be single or multiple When present in children such tumors cause more respiratory difficulty than they do in adults because of the greater relative impingement on the tracheal lumen

Tracheopathia Osteoplastica

This is one of the most interesting of the benign tumors of the trachea (Fig 6) It appears under the mucosa between the cartilaginous rings as a nodule composed of cartilage and bone In most cases the nodules are multiple and may involve the entire length of the trachea and extend down into the bronchi It is most likely to occur in the fifth and sixth decades of life Such tumors may produce symptoms that are dependent on their size number and distribution The condition may be recognized from roentgenologic examination especially tomographic studies



Fig 5 Aneurysm of the aorta invading the left main bronchus

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Amyloid tumor, xanthoma and chondroma occur with great rarity All five such tumors listed in the table give rise to symptoms

TREATMENT

The treatment of tracheal tumors depends largely on the type of lesion present The past 5 years have seen great advances in the surgical removal of a segment or portion of the wall of the trachea With this improvement in surgical technic, tumors that formerly had to be treated palliatively now can be removed in their entirety, with a good chance of cure

Carcinoma of the trachea, if the tumor has not infiltrated into contiguous structures or metastasized elsewhere, can be removed surgically, the continuity of the trachea being maintained by direct anastomosis or the use of a plastic or metal tube to replace the severed trachea The local excision of tumors such as cylindroma, with reconstruction of the tracheal wall, is being accomplished with increasing frequency If the tumor cannot be removed by excision, a great deal often can be accomplished by destruction of the tumor by electrocoagulation done directly through the bronchoscope or by means of tracheotomy The implantation of radon, the use of roentgen therapy, and exposure to the cobalt bomb have a definite place in the treatment of malignant lesions of the trachea

CHRONIC BRONCHITIS

Chronic bronchitis is a term frequently used as a "wastebasket' when a cause for chronic cough is not evident The condition actually exists, however, and is exceedingly common It consists of inflammation of the bronchial mucous membrane that is usually secondary to infections, such as the common cold, measles, whooping cough and influenza, or to inhaled irritants, such as cigaret smoke, farm or industrial dusts and chemical fumes Other conditions, such as bronchial asthma, may have an associated bronchitis with cough, conversely, chronic bronchitis with cough may be followed by bronchospasm or wheezing, commonly called asthmatic bronchitis Bronchiectasis, lung abscess or any suppurative process in the lungs may be associated with irritative bronchitis in those bronchi bathed with purulent secretion Purulent bronchitis may exist without permanent changes in the bronchi such as occur in bronchiectasis Bronchitis with cough may result from nocturnal aspiration of the contents of a pharyngoesophageal diverticulum or of material regurgitated from the esophagus in cardiospasm Aspiration of contents of the nasal passageways, such as oily nose drops or purulent material draining from infected paranasal sinuses, may cause the same type of irritative reaction on bronchial mucosa Finally, the mechanical irritation of the act of coughing is in itself capable of perpetuating bronchitis in many cases

DIAGNOSIS

Cough and expectoration are the chief symptoms Cough may be merely an occasional solitary expulsive effort or may be so severe that the patient has frequent prolonged paroxysms associated with laryngospasm These episodes may be terribly frightening to the uninitiated Anxiety with its associated hyperventilation may ensue and this may precipitate similar and more alarming paroxysms A "habit cough," or one not caused by any demonstrable disease, is frequently a deep rasping cough that may occur in severe paroxysms

Secretion may be absent, scant or profuse Mucoid sputum is described as clear, stringy or bubbly, and it may range from colorless ('white') to yellow Purulent sputum is thick or creamy and may be gray, gray green or yellow-green The physician should inspect a specimen of sputum if at all possible, rather than depend on the patient's description

The diagnosis of chronic bronchitis should be made only after other diseases such as tumors tuberculosis, fungous diseases, foreign bodies in the bronchus, congestive cardiac failure emphysema or any other disease ca-

pable of causing a cough have been excluded. The evaluation should include adequate historical information and physical examination. A roentgenogram of the thorax should be made to exclude other diseases as much as possible, and bronchoscopy often is necessary. When purulent sputum is present, bilateral bronchograms may be essential to exclude the possibility of bronchiectasis. Bacteriologic investigation of sputum is advisable not only to aid in excluding such conditions as tuberculosis and fungous diseases but because it may be of help in outlining treatment. The diagnosis of chronic bronchitis is hazardous without a thorough examination.

TREATMENT

The treatment of chronic bronchitis depends on elimination of the underlying cause. By all odds the commonest bronchial irritant is inhaled cigaret smoke. Thus any person with chronic bronchitis has a good chance of being helped by stopping the use of cigarets. One should eliminate other inciting irritants, however, whether these be inhaled, infectious or mechanical elements.

Chronic bronchitis frequently is perpetuated by the act of coughing itself, as already mentioned. Many patients believe they should do their best to cough up even tiny amounts of secretion and will make strenuous expulsive efforts to do so. Calm reassurance by the physician that nothing is seriously wrong and teaching patients the fallacy of this habit frequently suffice. The act of coughing may be compared to the rubbing of sandpaper up and down the inflamed air passages. Rest and freedom from irritation are required for the healing of most tissues, and thus pronounced "overcough" should be eliminated. Little tricks for the suppression of cough, such as the cessation of breathing when the "tickle" or other stimulus for coughing is first noted, may be helpful. The patient should concentrate on the suppression of cough rather than on an attempt to raise a small amount of mucoid secretion that is not an irritant.

Antitussive agents are chiefly narcotic drugs and should be avoided except for short term use. Codeine, dihydrocodeinone, methadone and dihydromorphinone hydrochloride (dilaudid) are the agents used most frequently. They usually are combined in a syrup with expectorants, such as potassium iodide or ammonia chloride, and may be helpful for temporary use in order to provide rest for the bronchial mucous membrane. Nonnarcotic agents such as carbetapentane citrate (toclase), caramiphen ethanedisulfonate (toryn) and dextromethorphan hydrobromide (romilar) are newer antitussive drugs. Thus far it has been difficult to evaluate their efficacy clinically. A person with nocturnal cough may benefit from sedation at bedtime in order to obtain two or three consecutive nights of rest and break his cycle or "habit" of coughing.

Expectorants are agents that are supposed to increase the volume and decrease the viscosity of sputum, making it resemble normal mucus, which is easily excreted by ciliary and normal bronchial action. These agents include potassium iodide, sodium iodide, ammonium chloride, antimony (as in brown mixture), terpin hydrate, ipecac and others. Their value is questionable and whatever effect is noted may be due to the water that is ingested at the same time. It may be superfluous to mention that adequate hydration with an intake of liquids that is greater than average is essential if one is to attempt liquefaction of secretions. Carbon dioxide given in a 5 to 10% mixture with 95 to 90% oxygen may increase the volume of sputum by increasing the rate and amplitude of respiration.

Bronchodilating agents such as ephedrine, aminophylline, isopropylarterenol (isuprel hydrochloride) and epinephrine may be helpful when cough is associated with bronchospasm or wheezing, as in asthmatic bronchitis. Ephedrine and aminophylline most commonly are taken orally but may be used as suppositories. The other two medications are commonly nebulized and inhaled. It is agreed that epinephrine is the more effective agent for relief of bronchospasm, but isopropylarterenol has fewer side effects and is preferable in most cases. Powdered forms of these medications are available, but in general are somewhat irritating to the bronchial mucous membranes. The action of these drugs

is not on the cough reflex itself, but the urge to cough diminishes as the violence of respiratory activity subsides

Antibiotics play a relatively minor role in the treatment of chronic bronchitis However, when purulent sputum is raised bacteriologic examination is indicated and appropriate antibiotics may be administered as in the treatment of bronchiectasis These antibiotics may be given orally, intramuscularly or by aerosolization

Fibrinolytic agents, such as streptokinase, streptodornase and trypsin, may have some usefulness when administered as an aerosol for inhalation Their purpose is the thinning of thick and sticky bronchial secretions These agents are seldom used at present in the treatment of chronic bronchitis

COMPLICATIONS

The complications of chronic bronchitis are principally those of the cough itself Nocturnal coughing disturbs the sleep of the patient and, perhaps more important, his family, making everyone annoyed and irritable Paroxysms of coughing may be so severe as to cause fracture of one or more ribs, the so-called cough fracture Emphysematous bullae may be produced or may enlarge These may rupture, producing pneumothorax or even mediastinal emphysema Subarachnoid or subconjunctival hemorrhage has occurred during a paroxysm of coughing Unconsciousness may ensue after a severe bout of coughing, this is commonly called "tussive syncope" or "laryngeal epilepsy." Actual syncope usually is preceded by a severe cough and then laryngospasm, which is manifested by a crowing sound Patients with such a reaction frequently can learn to stop the paroxysm short of fainting by holding their breath

Pulmonary emphysema is a common accompaniment of chronic asthmatic bronchitis In fact, the two are seen together so commonly that it is frequently difficult to tell when emphysema has begun during the course of bronchitis Studies of pulmonary function after adequate use of a bronchodilator may help to determine how much irreversible change is present The possibility of pulmonary emphysema is perhaps the main reason that one should attempt to eliminate chronic bronchitis or any chronic cough

BRONCHIECTASIS

Bronchiectasis is an inflammatory disease of the bronchopulmonary tree characterized by dilatation and partial destruction of the bronchial wall In addition, parenchymal changes usually occur in the pulmonary segments served by these bronchi The disease is becoming less common and it is generally conceded that this decreased incidence is largely due to the availability of antibiotics for treatment of pulmonary infections

ETIOLOGY

Although Laennec first described bronchiectasis almost 150 years ago, the pathogenesis in all cases is not known with certainty

Bronchial obstruction and its resultant inflammatory process in the bronchial walls and pulmonary tissues are factors common to most cases of bronchiectasis This obstruction is obvious when bronchiectasis is associated with inhaled foreign bodies, endobronchial tumors, cicatricial bronchial stenosis or bronchial compression from lymph nodes Bronchial glands continue to secrete mucus that cannot be expelled, and the bronchus dilates Whether this dilatation becomes permanent depends on the amount of damage to the bronchial wall, which depends in turn on the duration of obstruction and the amount of inflammatory reaction in the bronchus and surrounding parenchymal tissue

Bacterial and viral pneumonitis are common antecedents of bronchiectasis The factor of bronchial obstruction, even though not so obvious, is still present in association with parenchymal inflammatory disease The mucosa of inflamed bronchi may swell sufficiently to block the passageways Plugs of mucopurulent secretion may obstruct small or

large bronchi which then become dilated. This dilatation may revert to normal (pseudo bronchiectasis) or may progress to permanent bronchiectasis. The onset of the disease frequently can be traced to attacks of measles or pertussis or to the severe influenza epidemic of 1918 and 1919 in this country.

Aspirational pneumonia may result in bronchiectasis and presents the combination of bronchial obstruction and infection. Tonsillectomy, dental extractions or any operation in the nose, mouth or pharynx is fraught with the danger of aspirational pneumonitis or abscess. The same may be said for any abdominal operation with manipulation of organs of the upper intestinal tract; regurgitation and aspiration of gastric contents commonly occur. Esophageal disorders such as achalasia (cardiospasm) and pharyngo esophageal diverticulum are associated with nocturnal regurgitation and aspiration of contents of the esophagus or pouch causing pneumonitis and bronchiectasis. Users of oily nasal drops or those who take mineral oil just before going to bed are candidates for development of lipoid pneumonitis and bronchiectasis.

Sinusitis is frequently found in association with bronchiectasis but it is probably a complication rather than a causal factor. Most patients with this association have noted symptoms of bronchiectasis before those of sinusitis. However, the exact relationship is not completely clear.

Kartagener's syndrome is a triad of bronchiectasis, sinusitis and situs inversus. Originally described by Kartagener, others have concluded that bronchiectasis occurs in 15 to 20 % of all patients with dextrocardia.

Cystic fibrosis of the pancreas is frequently accompanied by bronchiectasis. The secretions are thick, sticky and viscid and the term "mucoviscidosis" has been applied to the disease. It is a diffuse process involving all lobes and may progress to generalized obstructive emphysema. Respiratory symptoms and recurrent episodes of pneumonia are often the most predominant features.

Agammaglobulinemia is a disturbance of the immunologic response of a person usually resulting in a chronic or recurrent suppurative process. Bronchiectasis has been demonstrated in approximately 20% of the reported cases.

Healed tuberculosis, lung abscess and other pulmonary suppurative processes may cause residual bronchiectasis.

PATHOLOGY

The fundamental changes in bronchiectasis are those of inflammatory destruction of peripheral bronchi which are not only dilated but lengthened and thickened. Variable amounts of parenchymal involvement of the lung occur from chronic interstitial and alveolar pneumonitis which may result in fibrosis and contraction of that portion of the lung.

The bronchial mucosa may show ulceration or metaplasia with loss of cilia and a tendency to squamatization. The submucosa is infiltrated by inflammatory cells and a variable amount of fibrosis. The mucosal glands may decrease in number. The musculature, elastic tissue and cartilage of the bronchial wall are destroyed to varying degrees. Changes in the blood vessels are frequent and consist of endarteritis. Enlarged inflammatory lymph nodes may surround major bronchi serving bronchiectatic lungs.

CLINICAL FEATURES

Cough with production of purulent sputum is the predominant symptom. The amount of sputum varies greatly from none at all, such as in "dry bronchiectasis," to a cup or more daily. Its purulent character is described variously as thick and yellow, yellow green, gray green or green. It may be malodorous. One glimpse of the sputum is much more valuable than a description. If sputum is not readily expectorated the physician should not hesitate to obtain some by the use of postural drainage of the bronchi. This is most easily performed by having the patient kneel on a chair or davenport placing the hands on the floor and staying in this position for a minute or so. Children and women sometimes have difficulty expectorating sputum for examination because of their habit of swallowing anything coughed.

Prolonged cough and sputum after a com-

mon cold are frequent in patients who have bronchiectasis Some state they have no cough except for one that persists 1 or 2 months after an ordinary upper respiratory infection

Frequent episodes of pneumonia and pleuritic pain should make one suspicious of the presence of bronchiectasis especially if repeated roentgenograms show the pneumonitis in the same location or if pleuritic pain is always on the same side

Hemoptysis is common and varies from slight streaking in sputum to a pinkish homogeneously colored specimen to frank hemoptysis of a cup or more of blood Fatal hemorrhage is rare Hemoptysis frequently is produced by overexertion and often is associated with acute infection of the respiratory tract It is typical of upper lobe bronchiectasis and dry bronchiectasis of the other lobes to have recurrent hemoptysis as the only symptom

Dyspnea and cyanosis in association with bronchiectasis may mean extensive disease or may be indicative of the development of emphysema late in the course of the disease They are ominous manifestations Lassitude fatigability malaise anorexia and loss of weight are manifestations seen in almost any chronic infection Metastatic abscesses in other portions of the body such as the brain are uncommon since antibiotics have become available

Pulmonary osteoarthropathy is indicative of long standing disease when associated with bronchiectasis Its exact cause is unknown but it is most commonly manifested by clubbing of the fingers and toes Tenderness may be present along some of the long bones such as the tibia as the result of periosteal proliferation

ROENTGENOGRAPHIC FEATURES

Several features in stereoscopic posteroanterior views of the thorax are suggestive of bronchiectasis These signs are not pathognomonic of the disease however the more of them that are present the more certain one can be of the diagnosis

Increased pulmonary markings are the most common of these features They consist of linear shadows extending from the hilus in a direction corresponding to the distribution of the bronchial tree They may be due to fibrotic changes in the bronchial wall and surrounding tissue or they may reflect the collection of purulent secretion in the bronchus They are the least dependable of the roentgenologic signs because they are found in other conditions such as congestive cardiac failure and because it is extremely difficult to make the distinction between normal and slightly increased markings

Chronic pneumonitis is found less frequently and usually is associated with the other features Honeycombing or ring shadows may be seen in any type of pulmonary fibrosis with secondary emphysematous air sacs but sometimes occur in bronchiectasis

Contraction of a portion of the lung such as an atelectatic or collapsed lobe is sometimes due to bronchiectasis When the right middle lobe is involved a hazy triangular shadow extends laterally from just below the hilus On the lateral roentgenogram a dense linear shadow extends diagonally anteriorly and downward from the hilus When either lower lobe is collapsed a dense triangular shadow is seen in the cardiophrenic angle On the left this is usually superimposed on the cardiac silhouette on the right the cardiac border merely may appear to be straightened The lateral view shows only a diffuse haziness in the region of the lower lobe

BRONCHOSCOPIC AND BRONCHOGRAPHIC FEATURES

The diagnosis of bronchiectasis is made with a reasonable degree of certainty by bronchography However before an opaque medium is instilled into the tracheobronchial tree it is wise to do a bronchoscopic examination chiefly in order to exclude an obstructing lesion One frequently can determine the side from which most of the purulent secretion is coming Furthermore if bronchoscopy is done just prior to bronchography secretion may be aspirated to allow better filling by the opaque medium

Bronchograms are best performed with the patient under topical anesthesia but in chil

dren it is usually necessary to use general anesthesia. After adequate anesthetization of the pharynx, larynx, trachea and major bronchi a catheter may be introduced through the nasal passage into the trachea. An opaque medium may then be introduced into the bronchi with or without fluoroscopic guidance by positioning the patient so that each bronchus is filled. Omission of use of the fluoroscope is simpler for both patient and physician and proper positioning of the patient provides adequate filling of each segment.

The type of opaque medium used has varied. Powdered bismuth oxide was used as early as 1905 but it was not until 1922 that an iodized oil was used. For the next 25 or 30 years the iodized oils such as lipiodol (poppy seed oil), iodochlorol (peanut oil) and lipoiodine (sesame-seed oil) were the most commonly used media. Their chief disadvantage is their slow disappearance from the lung. These oils occasionally have produced lipoid pneumonitis or granulomas in the lung.

Water soluble media were introduced in 1918 and have the advantage of rapid roentgenologic disappearance. Within 2 hours one cannot tell roentgenologically whether an opaque medium has been given. They include a stable organic iodide, iodopyracet (diodrast) in sodium carboxymethylcellulose such as umbradil viscous B (Astra) and ioduron B (Cilag).

More recently propyliodone (dionosil) has been introduced in both aqueous and oily forms. It has the advantage of rapid roentgenologic disappearance (2 to 4 days) and the oily form is less irritating to the bronchi than is the water soluble form. At present this medium has gained wide acceptance.

Reactions of sensitivity occur occasionally with the use of any of these substances. Iodism manifested by malaise, slight fever, tender swelling of the salivary glands simulating mumps and lacrimation may appear within 4 to 6 hours; it usually disappears within 3 days. A shocklike reaction is most likely to occur in patients with known allergies. It appears within 20 to 40 minutes and sometimes is associated with a convulsive seizure. Epinephrine should be given immediately and a mixture of oxygen and helium should be



Fig. —. Normal bronchogram. a, Right side; b, Left side.

administered by mask to combat such reactions.

Technically satisfactory bronchograms should show filling of each segmental bronchus including the upper lobes. A standard system of nomenclature of bronchopulmonary segments is desirable and that suggested by Jackson and Huber is the most widely ac



Fig 8 Bronchographic appearance in bronchiectasis of the saccular type

cepted Alveolar filling with opaque medium is undesirable but should not be too disturbing, because it almost always means that the bronchi serving these alveoli are normal even though they may not be well seen Ideally, however, a normal bronchogram should resemble a tree without leaves ('winter tree pattern) rather than the "summer tree' pattern of alveolar filling (Fig 7)

Bronchiectasis may be demonstrated in a cylindric, cystic or saccular form (Fig 8) It is most common in the lower lobes but may occur in any segment In disease of the lower lobes, the superior segment is usually spared but the middle lobe on the right or the lingular segment on the left frequently may be involved The anterior segment of the right upper lobe is also commonly affected The right middle lobe may be the only portion of the lung affected and may be associated with the "middle lobe syndrome'

STUDIES OF PULMONARY FUNCTION

At present, physiologic studies of the lung appear to play a minor role in appraising a person with bronchiectasis The tests are not of diagnostic value but may be of help in evaluating the patient as a surgical risk In this regard, however, the exercise tolerance of the patient, the depth and vigor of respiration the forcefulness of the cough, and the diaphragmatic excursion as determined by percussion are just as helpful As a general rule, if the patient can perform a normal day's activity, studies of pulmonary function may not be useful except as a base line for post operative comparison Bronchospirometry, with evaluation of each lung separately, provides the most helpful data, especially if one is contemplating bilateral surgical procedures

SURGICAL TREATMENT

Permanent bronchiectasis can be eradicated only by surgical removal of the diseased portions of the lung This treatment should be given serious consideration in every adult who has unilateral disease and in many who have bilateral disease The mortality rate in properly selected and prepared patients operated on by experienced surgeons is only 1 or 2%

Indications for surgical treatment depend on the degree of symptoms age of the patient, extent of disease, and the desires of the patient When the disease is asymptomatic or when a localized zone of bronchiectasis is discovered in searching for the cause of slight hemoptysis, one should be reluctant to advise such a major operation When pulmonary suppuration or hemoptysis is moderate to severe or when recurrent pneumonitis and pleurisy are problems surgical intervention should be considered In patients less than 5 or more than 50 years of age, the operation should be entertained only under exceptional circumstances Those whose tolerance for exercise is limited usually have such extensive disease that surgical treatment is inadvisable The maximal amount of pulmonary tissue that should be considered for surgical removal is one entire lung or segments of two lungs totaling not more than those in one lung Some patients have had the right lower and middle lobes, the left lower lobe and the lingular segment of the left upper lobe removed,

but other factors such as age and general condition must be ideal in such patients or pulmonary function will be dangerously compromised. Sometimes in bilateral disease resection of the affected tissue on the side in which the greater amount of disease is located provides so much benefit that further resection either is inadvisable or is refused by the patient.

Preoperative preparation by postural drainage and administration of antibiotics is desirable to eliminate purulent bronchial secretions as much as possible at the time of operation. When lipiodol or iodochlorol is used for bronchography it is probably best to defer surgical treatment for 4 to 6 weeks or until evacuation of the medium is fairly complete. With the water soluble media or oily dionosil however such a delay does not appear to be necessary. Tracheotomy done either preoperatively or immediately postoperatively while the patient is still under anesthesia may be desirable when bronchial secretion is copious or when cough is weak.

The surgeon should remove the involved segments or lobes by careful dissection and individual ligation. The advisability of retaining the superior segment of the lower lobe rather than resecting it with the diseased basal segments when it is not involved by bronchiectasis is debatable; recent evidence indicates that postoperative complications might be increased by such retention but that long term results justify an attempt to save this segment.

MEDICAL TREATMENT

When surgical excision is not advisable palliative medical treatment should be given. The principal aim of this is to minimize the suppurative process or secondary infection as much as possible.

Good food, adequate rest, sufficient humidification of the home and avoidance of bronchial irritants such as tobacco smoke are helpful. Upper respiratory infections are deleterious to bronchiectatic patients and sometimes a change to a warm dry climate decreases the incidence of these. However dust commonly encountered in such a location may be enough of an irritant to produce an increase in bronchorrhea and a permanent change of residence should not be considered without a temporary trial. Sinusitis may require separate treatment but as a rule it is helped by controlling bronchiectasis with medications or by eliminating pulmonary suppuration by surgical intervention. Treatment of associated bronchial asthma may be necessary although frequently bronchiectasis is the "trigger mechanism."

Thinning of thick, viscid bronchial secretions may be desirable and can be done in various ways. An adequate intake of fluid is essential and may be supplemented by the use of iodides or ammonium chloride. Inhalation of steam or aerosolized solutions such as sterile water sometimes used as a diluent for antibiotics, wetting agents such as triton A 20 or proteolytic enzymes such as trypsin or streptokinase may loosen sticky secretions.

Postural drainage should be designed to evacuate properly the parts of the lung affected. Inasmuch as the lower lobes or the dependent portions of the lungs are involved most commonly the act of lying across a bed with elbows on the floor or kneeling on a davenport and placing the hands on the floor should allow secretion to be expelled by gravity. This should be done three or four times daily for 10 or 15 minutes at the beginning of treatment. Later the patient may become discouraged because he does not produce much sputum and is likely to stop. Rather he should decrease and increase the frequency of postural drainage in accordance with the amount of material available for expectoration.

Antibiotics combined with intermittent postural drainage are valuable aids in the treatment of bronchiectasis. Opinions vary concerning the amount and type of antibiotics to be used but all observers agree that their use has changed considerably the outlook of a bronchiectatic patient. In order to choose the proper medication it is best to know what organisms are present in the sputum. This is especially true if antibiotics have been given previously, thereby altering the flora. Once the predominant organisms are obtained by culture, their sensitivity to various antibiotics

can be determined in vitro and the "proper medication can be administered. However it must be admitted that dramatic response to the "proper" antibiotic is not always obtained in actual treatment of a patient and one is sometimes forced to try others.

Penicillin and broad spectrum antibiotics such as tetracycline are the agents employed most commonly at present. Penicillin may be used orally, parenterally or by aerosolization. Tetracycline usually is given orally. The amount necessary varies with each patient but in general it is best to start with a large dose such as 1 000 000 to 2 000 000 units of penicillin or 2 gm of tetracycline given daily in divided doses. Administration should be continued until the amount of sputum is greatly decreased and this period is usually not more than a week if effective postural drainage is used also. The length of the period may depend of course on the extent of disease, the amount of suppuration and the sensitivity of the organisms.

Other antibiotics such as streptomycin or dihydrostreptomycin and erythromycin may be indicated depending on the bacterial flora but these antimicrobial agents play a less important role.

The frequency with which administration of antibiotics is recommended varies among physicians. Some state that these agents should be saved for serious infections so that they will still be effective when needed. Others use moderately large doses for long periods feeling that much disability is prevented. Still others consider that certain medications such as the broad spectrum antibiotics suppress the usual flora allowing the emergence of organisms such as Pseudomonas aeruginosa or Bacillus proteus that have serious potentialities and that are more difficult to eradicate.

It is our opinion that antibiotics such as penicillin and tetracycline should be administered to patients who have bronchiectasis with each upper respiratory infection or common cold and that it is safe to use such agents intermittently for 4 or 5 days at a time to control copious suppuration which is annoying to the patient and his associates. The frequency of these periods of administration will vary from person to person and it is safe to let most of these patients regulate the interval between treatments if they are conscientious enough to use postural drainage diligently and wisely.

PROGNOSIS AND PREVENTION

Prior to the advent of surgical treatment and antibiotics patients who had bronchiectasis lived shortened and unhappy lives. Pneumonia, empyema, brain abscess and amyloidosis frequently were fatal complications. At present many patients with bronchiectasis survive with the subsequent development of pulmonary emphysema.

When surgical excision is possible however one can expect 75% of the patients to return to full vocational activity with few or no remaining symptoms. Surgical intervention commonly is recommended for bronchiectasis in children but a recent study showed that the results are not so good as they are in adult life. New lesions of bronchiectasis or zones of residual bronchiectasis are likely to be found after operation in a higher proportion of children than adults probably because of postoperative complications such as retention of secretions.

Bronchiectasis may be prevented by early removal of bronchial obstruction due to foreign bodies and by adequate prevention and treatment of pulmonary infections. Pertussis can be prevented by inoculation and measles frequently can be attenuated. Pneumonia and tuberculosis usually can be treated with effective chemotherapy and antibiotics.

FOREIGN BODIES IN THE TRACHEOBRONCHIAL TREE

The aspiration of a foreign body into the tracheobronchial tree usually is accompanied by such dramatic sequelae that the diagnosis in most cases is made with ease and bronchoscopic removal of the foreign body is advised. Unfortunately instances still remain in which prompt removal of the foreign body is not advised, there being a tendency to procrasti

rate in the hope that the foreign body will be coughed out The chance of such a termination is extremely remote The seriousness of permitting a foreign body to remain in the lung is well realized when it is pointed out that the mortality rate is more than 50% if *such a course is followed In contrast, the* mortality rate attendant on bronchoscopic removal of foreign bodies from the tracheobronchial tree in the hands of a skilled bronchoscopist is less than 1%

A more difficult problem is the recognition of the overlooked or forgotten aspirated foreign body It is surprising how frequently a patient may forget the incident during which he aspirated a foreign body The possibility of the presence of an aspirated foreign body must be kept in mind constantly in every instance of pulmonary suppuration and in cases in which unexplained wheeze is present (Fig 9) Unfortunately a typical diagnostic *picture for all instances of aspirated foreign* body does not exist. The sequence of events that usually follows aspiration of a foreign body varies with the character size and shape of the foreign body and the age of the patient. The initial act of aspirating a foreign body into the tracheobronchial tree generally is associated with a violent paroxysm of coughing and less frequently wheezing Unless the foreign body is of such size as to produce interference with respiration a period generally follows in which the patient is free of pulmonary symptoms This asymptomatic period varies in duration and may last for several hours or even for years dependent again on the character and size of the foreign body It is during this period that the foreign body is most likely to be overlooked The late symptoms of an aspirated foreign body are usually those of pulmonary suppurative disease namely cough expectoration hemoptysis and occasionally wheeze

Vegetable foreign matter is more likely to cause severe and acute pulmonary damage than are metallic foreign bodies Vegetable foreign bodies produce severe bronchitis which is characterized by rapid accumulation of thick purulent secretion and pronounced hyperemia swelling and edema of the bronchial mucosa The bronchi distal to the point



Fig 9 Pulmonary suppuration due to an aspirated foreign body (bone) The patient did not recall aspirating the foreign body Inset the foreign body



Fig 10 Roentgenographic appearance in a case in which a foreign body had been present in a bronchus for 17 years.

of the foreign body tend to fill with purulent exudate

A nonobstructive foreign body may remain dormant in a bronchus for months or even years without producing any appreciable degree of pathologic change in the bronchial tube (Fig 10) This delay in effect is frequent when straight pins have been aspirated into the bronchi Corrosion and mechanical irritation eventually lead to the development of obstruction of the bronchus and concomitant secondary pulmonary suppuration If a foreign body, especially of metallic material, is allowed to remain in the bronchus for a long period, a stricture generally will develop at the site where the foreign body has lodged With time, the bronchus below the site of the stricture tends to dilate and the foreign body may drop into this dilated bronchus This is technically important in removal of an aspirated foreign body from the bronchial tree because, when it takes place, dilation of the stricture is necessary before the foreign body can be safely withdrawn from the bronchus

The physical findings on examination of the thorax in cases of aspirated tracheobronchial foreign body vary with the size, character and location of the foreign body, and with the degree and character of bronchial obstruction produced In addition, secondary suppurative changes may greatly alter the physical findings In the interpretation of physical findings in cases of foreign body in the tracheobronchial tree, it must be recalled that the bronchi are not static tubes but constantly change in size and length during respiration As a result, constant variations exist in the ease with which air can pass through the bronchus and about the foreign body during respiration

The bronchial obstruction resulting from aspirated foreign bodies has been described by Jackson and Jackson as of four types, a classification that is of special value in the interpretation of physical findings

Type 1: Partial Bronchial Obstruction. This type of obstruction is manifested by interference with free passage of air through the bronchus in which the foreign body is lodged and interference with normal drainage of the bronchus distal to the point of obstruction As a consequence, limitation of expansion of the lung on the side of involvement is present On percussion, slight impairment in resonance may be noted over the thorax in the region below the point of bronchial obstruction Auscultation may reveal harsh blowing respiratory sounds with passage of air about the foreign body The respiratory sounds are diminished over the region of increased dullness, vocal and tactile fremitus may be impaired, and rales are often present

Type 2: Expiratory Check-Valve Obstruction. Interference with free egress of air during expiration is the characteristic of this type of obstruction This is especially likely to occur in the presence of round foreign bodies of vegetable matter With expiration, the bronchus narrows, closing about the foreign body and thus interfering with the expulsion of air As a result, the lung in which the obstruction exists becomes overdistended with air and shows great limitation of expansion Percussion over the involved lung reveals tympanitic sounds Respiratory sounds are diminished or absent Rales are not heard on the invaded side, although they may be present on the free side Vocal resonance and fremitus are altered but little

Type 3. Complete Bronchial Obstruction This type is characterized by interference with entrance of air into the lung beyond the point of obstruction The air that was in the lung distal to the obstruction is soon absorbed, and secretions rapidly accumulate on the side of involvement, producing the typical picture of atelectasis As a result, limitation of expansion, great impairment of the percussion note, and an absence of respiratory sounds and of rales are noted in the involved lung The heart usually shifts toward the side of involvement, and the diaphragm is elevated on this side Compensatory emphysema is present on the free side

Type 4· Inspiratory Check-Valve Obstruction. This form of obstruction is the reverse of type 2 and probably immediately precedes type 3 It is of extremely short duration and little practical significance

ROENTGENOGRAPHIC STUDIES

Roentgenographic examination of the lungs

should be done in all cases in which aspiration of a foreign body is suspected. In addition to the routine anteroposterior and lateral thoracic roentgenograms it is recommended that roentgenograms be made at the end of both inspiration and expiration.

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The bronchial obstruction resulting from aspirated foreign bodies has been described by Jackson and Jackson as of four types a classification that is of special value in the interpretation of physical findings

Type 1 Partial Bronchial Obstruction This type of obstruction is manifested by interference with free passage of air through the bronchus in which the foreign body is lodged and interference with normal drainage of the *bronchus distal to the point of obstruction* As a consequence limitation of expansion of the lung on the side of involvement is present On percussion slight impairment in resonance may be noted over the thorax in the region below the point of bronchial obstruction Auscultation may reveal harsh blowing respiratory sounds with passage of air about the foreign body The respiratory sounds are diminished over the region of increased dullness vocal and tactile fremitus may be impaired and rales are often present

Type 2 Expiratory Check Valve Obstruction Interference with free egress of air during expiration is the characteristic of this type of obstruction This is especially likely to occur in the presence of round foreign bodies of vegetable matter With expiration the bronchus narrows closing about the foreign body and thus interfering with the expulsion of air As a result the lung in which the obstruction exists becomes overdistended with air and shows great limitation of expansion Percussion over the involved lung reveals tympanitic sounds Respiratory *sounds are diminished or absent Rales are* not heard on the invaded side although they may be present on the free side Vocal resonance and fremitus are altered but little

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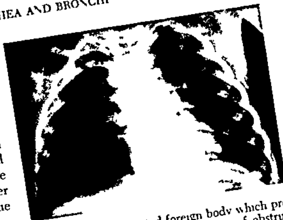
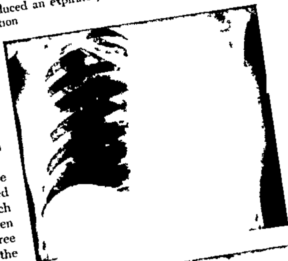


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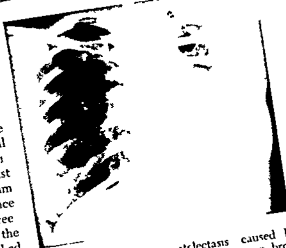


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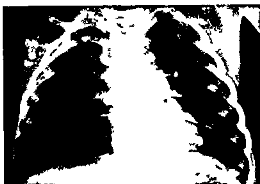


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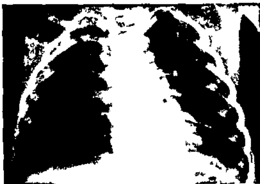


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Fig. 12. Obstructive atelectasis caused by polypoid adenocarcinoma of the left main bronchus treated successfully through the bronchoscope. a, Before treatment. b, After treatment.

examination should be done without the advantage of full and careful clinical study under the best possible circumstances The practice of inverting the patient in an attempt to dislodge the foreign body from the tracheobronchial tree is to be condemned as unsafe as the change of position may dislodge the foreign body so that it may become wedged in the glottis resulting in spasm and complete asphyxia of the patient Although safe removal of a foreign body at the first bronchoscopy can be accomplished in practically all cases a second or third bronchoscopy occasionally may be required

A characteristic of an aspirated foreign body in the tracheobronchial tree *is that in most* cases even after the foreign body has been in the lung for a considerable length of time and has set up extensive pathologic *processes* the difficulty will clear up promptly on removal of the foreign body

TUBERCULOSIS OF THE TRACHEOBRONCHIAL TREE

Tuberculosis of the trachea and bronchi has been recognized for many years According to Smart Richard Morton in 1694 was probably the first to describe lesions of the *bronchi due to tuberculosis Since then* numerous reports based primarily on necropsy studies have appeared It has been only in the past 2 or 3 decades with the more wide spread use of the bronchoscope as a diagnostic aid in the study of pulmonary disease that the true clinical significance of the disease has been appreciated The advent of thoracic surgery and the introduction of antituberculotic drugs in the treatment of pulmonary tuberculosis have added immeasurably to knowledge concerning its development cause and complications

A difference of opinion exists among observers as to the incidence of tuberculous tracheobronchitis It has been stated that it occurs in from 10 to 60% of all cases of pulmonary tuberculosis This discrepancy as to incidence is chiefly dependent on whether the observations are based on bronchoscopic appearance alone or on the study of operative or necropsy material To a lesser extent the discrepancy depends on the state of advancement of the pulmonary tuberculosis in the particular group of cases reported Although tuberculous tracheobronchitis is more likely to be present in advanced pulmonary tuberculosis than in early disease it may occur at any stage

The manner in which the trachea and bronchi become involved in the tuberculous process has not been definitely established they are seldom the primary site of the disease Experience indicates that tuberculosis of the trachea and bronchi may develop through a number of routes In the first place tuberculosis may spread to the bronchi and trachea by way of the lymphatic system into the mucous glands The lymphatic structures surrounding the major bronchi the trachea and the mediastinum absorb infected material from the periphery of the lung As a result of the close contact of the mucous glands with diseased lymphatic tissues the glands are attacked and thus carry infected material through the walls of the bronchi into the mucous membrane Secondly the disease may extend directly to the bronchus or trachea from neighboring tuberculous tissue *Thirdly* direct implantation may occur from infected sputum or secretions such as accompany the discharge from a tuberculous focus into a bronchus

PATHOLOGIC ASPECTS

The bronchoscopic appearance of the lesions of tuberculous tracheobronchitis varies with the particular form taken by the disease and its stage of development In children the *earliest bronchoscopic findings are usually* those produced by enlargement of mediastinal tracheal and bronchial lymph nodes which impinge on the tracheobronchial tree and cause fixation and narrowing of the airway In contrast the earliest findings in adults con*sist of reddening and edema of the* mucous membrane these changes may be diffuse but



Fig 13 Tuberculous ulcer of trachea and bronchi

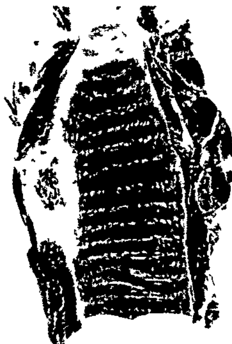


Fig 14 Tuberculoma of trachea

more often are localized to a small region situated about or opposite the opening of the bronchus The reddened mucosa soon assumes a granular appearance due to the multiple small discrete tubercles in the submucosa (Fig 13) Such an infiltrative process may undergo resolution and leave little evidence of its previous existence or it may go on to the hyperplastic or ulcerative form

The hyperplastic form is characterized by thickening of the bronchial mucous membrane associated with submucosal lymphocytic infiltration The mucous membrane is less flexible with a decrease in the diameter of the bronchial or tracheal lumen The submucosal tubercles tend to conglomerate This may go on to the formation of a tuberculoma that protrudes into the lumen of the bronchus and presents the appearance of a benign tumor (Fig 14)

In the ulcerative form small pin point zones of ulceration appear It is difficult at first to distinguish these small ulcers from flecks of mucus The small ulcers tend to coalesce and fuse forming larger zones of ulceration that vary in size perhaps involving the entire circumference of the trachea or bronchus The edge of the ulcerated region is generally ragged and the base is covered with a dirty grayish exudate Granulation tissue which generally is regarded as indicative of ulceration is frequently present and projects into the lumen of the trachea or bronchus presenting the appearance of a tumor and sometimes completely obliterating the zone of ulceration The tendency of the ulcerative hyperplastic process is to heal and this may lead to fibrostenosis

The fibrostenotic stage is characterized by narrowing of the lumen of a bronchus or the trachea The stenotic zone is firm and the lumen may be reduced to a pin point opening The mucous membrane overlying the stricture may be smooth or may exhibit several areas of ulceration or granulation The stenosis occurs usually as the result of healing of tuberculous ulceration less frequently it results from localized submucosal infiltration Purulent material usually exudes from the stenotic opening When the cause of the stricture is not clear it is advisable to aspirate secretion from below the stricture for examination for acid fast organisms and fungi since proof of the cause of the lesion often can be thus obtained (Fig 15)

Tuberculosis of the hilar and tracheal lymph nodes may lead to changes in the trachea and bronchi that may produce clinical symptoms This is especially common in infants and



Fig 15 Atelectasis due to tuberculous stricture



Fig 16 Deformity of lower end of trachea due to a tuberculous node

young children *Continued pressure* on the bronchus or trachea is accompanied by an inflammatory reaction in the mucous membrane overlying the tuberculotic node The mucous membrane which at first appears congested gradually becomes paler in color and thinned out. At this stage *determination of* the cause underlying the process may be impossible Although the lesion may retrogress at this stage without perforation of the tracheal or bronchial wall the node or its contents more frequently may rupture into the lumen of the tracheobronchial tree and be evacuated (Fig 16) If the patient is examined at this stage the opening through the wall of the trachea or bronchus can be seen readily Study of tissue or secretions obtained from the opening may lead to the correct diagnosis An anthracotic node may produce a similar picture As a rule after the node or its contents have been evacuated into a bronchus or the trachea the entire process may subside or a small pitting scar may be left at the site of the perforation However should evacuation take place into the esophagus at the same time an esophagotracheal or esophagobronchial fistula may be formed

SIGNS AND SYMPTOMS

Although tuberculous tracheobronchitis may produce a definite train of clinical symptoms these symptoms are not necessarily characteristic of tuberculosis but may be produced by carcinoma benign tumors foreign bodies or other lesions

Partial stenosis of the tracheobronchial tree causes a wheezing stridulous type of respiration that is especially noticeable with exertion or speech and when the patient is recumbent The patient may have attacks of asthma and increased dyspnea with exertion Dependent on the degree of bronchial obstruction variations may occur in the amount of sputum Fever may be present when there is interference with drainage of secretions with evacuation of the retained secretions the fever subsides promptly Ormerod stated that pain which generally is aggravated by coughing is frequently present behind the sternum in ulcerative tuberculosis of the trachea and bronchi Bleeding may occur Warren and associates found evidence of tuberculous bronchial ulceration or stenosis in 57% of the cases

of pulmonary tuberculosis in which the aforementioned train of symptoms was present

The physical findings in tuberculous tracheobronchitis also depend on the degree of mechanical obstruction present in the tracheobronchial tree Atelectasis of one or more lobes may result from obstruction caused by stricture or tuberculoma (Fig 17) The presence of atelectasis especially atelectasis that fluctuates in degree should strongly suggest *tuberculous tracheobronchitis of the ball valve type*

McIndoe and co-workers stated that the roentgenologic findings of importance in suggesting tuberculous tracheobronchitis include (1) the presence of atelectasis especially if fluctuating (2) a tendency to unexpected and unexplained spread of the disease and (3) evidence of a partially obstructed cavity with a fluid level While these findings are not pathognomonic of tuberculous tracheobronchitis they are strong presumptive evidence in the face of active pulmonary tuberculosis Of all these atelectasis is by far the most significant

INDICATIONS AND CONTRAINDICATIONS FOR BRONCHOSCOPY

It has become a routine procedure in many sanatoriums to perform bronchoscopy on all patients at the time of their admission except when some contraindication is present On the other hand such authors as Samson have stated that this procedure is not indicated unless the patients present symptoms indicative of tuberculous tracheobronchitis for in their experience such lesions seldom will be found in the absence of a characteristic syndrome *The problem is not so simple or clear cut however* when the physician s experience is not limited to the care of patients with tuberculosis

Bronchoscopy should be employed (1) in any case of pulmonary tuberculosis associated with wheeze stridor evidence of atelectasis obstructive emphysema or variations in sputum with associated symptoms that might suggest bronchial obstruction (2) in any case in which a question exists as to the accuracy of the diagnosis of tuberculosis (3) *in any case* in which the patient continues to have sputum containing tubercle bacilli in spite of the fact that the pulmonary lesion apparently has been controlled by artificial pneumothorax or thoracoplasty (4) in event of spread of the disease to a healthy lung when such a complication *is not expected on the basis of the existing*



Fig 17 Atelectasis of the right middle lobe caused by tuberculosis a Posteroanterior view b Lateral view

pulmonary condition, and (5) as a routine procedure in all cases of pulmonary tuberculosis in which resection of the lung or thoracoplasty is undertaken It has been amply demonstrated that the operative results will be far superior if an intact mucous membrane exists than if such is not the case, even though the bronchial wall itself may continue to harbor tuberculous disease in spite of mucosal healing

Comparatively few contraindications to bronchoscopy are present in pulmonary tuberculosis If the procedure is done with caution, it rarely aggravates the disease Bronchoscopy should not be done (1) in the presence of acute laryngeal tuberculosis, (2) on a patient with pulmonary tuberculosis who has had recent extensive pulmonary hemorrhage, or (3) on a patient who has far-advanced tuberculosis and who has toxemia and cachexia

TREATMENT

The introduction of antituberculotic drugs in the treatment of pulmonary tuberculosis has changed completely the former concept of treatment of this disease In most instances, a tuberculous process involving the trachea and bronchus will respond to such drug therapy with fairly rapid epithelial healing The maximal benefits in bronchial and tracheal lesions to be obtained by chemotherapy usually are evident within 6 to 12 months When surgical treatment is to be undertaken in pulmonary tuberculosis, it is well to adhere strictly to the rule that the most satisfactory results are obtained with a quiescent bronchus

In those instances in which a fibrostenotic lesion has been brought under control, much progress has been made in dealing with such a lesion by means of plastic surgical procedures on the trachea or bronchus, along with resection When obstruction is caused by pressure from a tuberculous lymph node, a satisfactory response to drug therapy also may be anticipated Only on rare occasions will surgical measures be required

BRONCHOGENIC CARCINOMA

Bronchogenic carcinoma accounts for more than 10% of all carcinomas in the human body Like carcinoma elsewhere in the body, it is prone to occur primarily in persons who are more than 40 years of age It occurs about eight times as frequently in men as in women

SYMPTOMS

Unfortunately, carcinoma of the lung is often so insidious in its onset and so rapid in its development that its earliest manifestations may be produced by extension of the tumor or by metastasis The symptoms depend in large measure on the location of the tumor, its size, the degree of bronchial obstruction and the presence of secondary infection beyond the site of bronchial obstruction Tumors that arise in the periphery of the lung and are small seldom produce symptoms However, the majority of lesions originate in the larger bronchi and tend to cause symptoms

Cough is usually the earliest and commonest symptom in carcinoma of the lung, being present in 85% of patients It is often extremely difficult to evaluate this symptom because such a large percentage of the patients smoke cigarets and cough is such a prevalent finding in smokers The onset of cough or a change in the character of cough in a middle-aged person always should cause concern At first, when the tumor is small, the cough is usually dry and nonproductive, as the tumor increases in size, producing interference in drainage of the bronchus and secondary infection beyond the point of obstruction, the cough becomes productive of mucoid or mucopurulent secretion

Ulceration invariably occurs with an enlarging carcinomatous process and often causes bleeding, which is present in at least 50% of patients who have carcinoma of the lung (Fig 18) The bleeding generally is not profuse, often producing only streaking of the sputum

Although loss of weight seldom is referred

to is of diagnostic significance in carcinoma of the lung it is common in this disease More than two thirds of patients who have carcinoma of the lung show evidence of loss of weight Weakness often goes hand in hand with this loss

Approximately one half of patients who have carcinoma of the lung complain of some discomfort or fullness in the thorax The longer the tumor has been present the more likely is this symptom to occur Severe pain is not common but when present is usually indicative of direct extension of the growth into the thoracic wall pleura or mediastinum Constant dull pain in the back causes one to suspect mediastinal invasion or extension into the spinal column Pain extending down either arm usually indicates involvement of intercostal nerves or the brachial plexus

Dyspnea is common in bronchogenic carcinoma but usually appears late in the course of the disease Its severity largely depends on the site of the tumor the degree of bronchial obstruction and extent of secondary suppuration When pleural effusion occurs the degree of dyspnea invariably increases Wheezing respiration is noted by the patient or detected at the time of examination in approximately 10 per cent of cases It is more likely to occur late in the disease although in rare instances it may be the initial symptom

Hoarseness is not common in carcinoma of the lung but when present is indicative of spread of the tumor to the mediastinum with impingement on the recurrent laryngeal nerve The possibility of carcinoma of the lung must be ruled out in any case of unexplained hoarseness

Symptoms of Secondary Infection

With increase in size of the bronchial growth and interference with normal drainage infection of the bronchial tree beyond the growth invariably takes place This infection may be nothing more than bronchitis or it may develop into bronchiectasis pneumonitis pulmonary abscess pulmonary gangrene or empyema Such infections because of improper drainage frequently cause recurrent bouts of chills and fever that may last from 3 to 5 days Any so-called pneumonia that does not clear

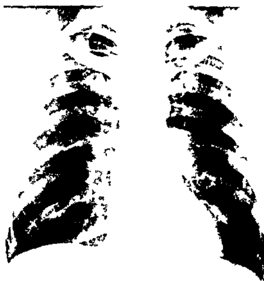


Fig 18 Carcinoma of the lung with hemoptysis

up promptly should be looked on with great suspicion and every effort should be made to exclude the possibility of an underlying carcinoma "Flu from which recovery is extremely slow in a patient past middle age should be regarded with suspicion Unexplained pulmonary abscesses or empyema should be placed in the same category

CLINICAL FINDINGS

The physical findings in primary carcinoma of the bronchus depend on the situation of the tumor its size the degree of bronchial obstruction the presence of secondary inflammatory changes and the amount of pleural involvement A small lesion in the periphery of the lung or in a large bronchus may escape detection even with the most careful examination and may be discovered only accidentally during the course of bronchoscopy or more likely on roentgenologic examination (Fig 19)

An all too frequent tendency exists to neglect physical examination of the thorax or to disregard completely its results in evaluating the problem of bronchogenic carcinoma Although it is true that results of physical examination of the thorax often are inconclusive or show nothing abnormal the procedure



Fig 19 Circumscribed lesion of bronchogenic carcinoma with shadow superimposed on the anterior end of the left second rib

never should be omitted It is only by paying meticulous care to all diagnostic aids that progress can be made in prompt and early recognition of these lesions This examination also may add information that influences the physician in selecting the most suitable treatment

A most valuable but frequently neglected aid in physical diagnosis is inspection of the thorax with the patient recumbent Often such inspection discloses that one side of the thorax lags behind its mate on inspiration which should cause one to suspect the presence of an intrapulmonary lesion on the affected side Special attention should be directed to the presence of a wheeze This can be elicited best by having the recumbent patient breathe with the mouth open If the tumor or the region of pulmonary atelectasis produced by the tumor is close to the thoracic wall dullness on percussion may be found over the involved portion The most important finding on auscultation is suppression of breath sounds over the region of involvement When secondary infection has developed and bronchial obstruction is not complete scattered coarse rales may be associated with suppression of breath sounds Fluid in the pleural cavity completely obscures the foregoing findings and only dullness or flatness on percussion with suppression or absence of breath sounds may be noted

Clubbing of the fingers in a patient more than 40 years of age especially when of recent onset and noted in connection with thoracic disease of short duration should cause one to suspect the presence of pulmonary carcinoma after the possibility of empyema has been excluded

A careful search for metastatic lesions in lymph nodes is obligatory in every case of suspected pulmonary carcinoma The supraclavicular regions and the axillae must be palpated carefully for enlarged and firm lymph nodes An undiagnosed pulmonary lesion that has been present for months often can be diagnosed correctly by the simple procedure of identifying a hard lymph node in the supraclavicular region or axilla This finding often alters the problem of treatment

When a tumor arises in the apex of the lung which is the so called superior sulcus tumor (Pancoast's tumor) Horner's syndrome may be present on the homolateral side some atrophy of the muscles of the hand and arm may be present on the same side These findings result from invasion of the tumor from the apex of the lung into the supraclavicular fossa and mediastinum with involvement of



Fig 20 Superior sulcus tumor (Pancoast's tumor) in apex of left lung

the sympathetic chain and the brachial plexus (Fig 20)

ROENTGENOLOGIC FEATURES

Roentgenologic examination of the thorax is of great value in the diagnosis of carcinoma of the lung Unfortunately the classic signs of bronchogenic carcinoma usually are produced by changes present late in the disease From the diagnostic standpoint it is useful to consider the development of bronchial carcinoma as occurring in either a peripheral small bronchus or a central large portion of the bronchial tree The signs of disease may be those of the actual mass itself or those produced by the effects of the mass namely those of bronchial obstruction A peripheral mass growing primarily extraluminally may present a fairly discrete outline It may be stated that if the mass contains evidence of calcification especially if it appears laminated or like popcorn it is not due to bronchogenic carcinoma

In more centrally located lesions small non obstructing intraluminal carcinomas are not apparent on examination of usual roentgenograms of the thorax If the presence of such lesions is suspected but they cannot be found by means of bronchoscopy they may be located by the skillful use of body section roentgenography or by bronchography The former method may reveal unrecognized bronchial occlusion unsuspected cavitation or enlargement of paratracheal and hilar lymph nodes it may aid in the differentiation between a solid tumor and a collapsed segment of lung Bronchography may reveal either intrabronchial or extrabronchial lesions

There are no cardinal roentgenologic signs of carcinoma of the bronchus because the features change with continuing growth of the lesion However when a large bronchopulmonary segment becomes obstructed one may detect diminution in volume of the portion of lung affected together with increased radiodensity resulting from loss of air and accumulation of secretions (Figs 21 and 22) If major bronchi are involved there may be elevation of the diaphragm narrowing of the intercostal spaces spreading of the shadows of the uninvolved vascular and bronchial structures on the affected side and a shift of the mediastinum to that side



Fig 21 Primary carcinoma of bronchus producing localized atelectasis

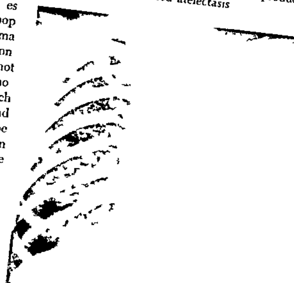


Fig 22 Carcinoma of the lung with pronounced roentgenographic changes

In the later stages of development of central tumors the growth characteristics of the particular tumor and the associated inflammatory changes have great effect on the roentgenologic features Thus a tumor spreading peripherally through lymphatic channels may present a poorly defined peripheral border or a reticu



Fig 23 Late stage of a central bronchogenic carcinoma Note poorly defined border

lated appearance (Fig 23) Large hilar *masses bordered by clear lung or bilateral* paramediastinal masses are more likely to be caused by mediastinal tumors than by bronchial carcinomas although the former may produce bronchial obstruction by extrinsic pressure

It is not always possible to differentiate a cavitating carcinoma of the lung and a pulmonary abscess (Fig 24) Actually the former may be considered as a special example of the latter A thick wall with an irregular poorly defined interior surface and a relatively *well* defined external outline has been considered to favor the diagnosis of a *cavitating neoplasm* (Fig 25) However a cavitating neoplasm at *times also may present roentgenologic evi*dence of a classic benign pulmonary abscess with a relatively smooth interior outline and a less well demarcated external contour that may fade imperceptibly into the poorly defined shadow of an inflammatory process

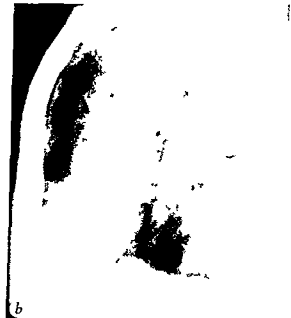


Fig 24 *Cavitating squamous cell carcinoma* of lung resembling abscess Note fluid level a Anteroposterior view b Lateral view

PATHOLOGIC ASPECTS

It has been recognized for a *long* time that bronchogenic carcinoma varies greatly in its clinical manifestations and its operability and resectability The factor that appears to be most responsible for these characteristics is the cellular type of the tumor itself

Bronchogenic carcinoma may be divided into various groups depending on the type of *cells involved McDonald and associates*

classified bronchogenic carcinoma into four groups namely (1) small cell carcinoma (2) adenocarcinoma (3) squamous cell carcinoma and (4) large cell carcinoma Some bronchogenic carcinomas are not made up of a single cellular type but have a mixed histopathologic pattern Parts of the same tumor may be made up of different cellular types

In a study of 767 proved bronchogenic carcinomas seen at the Mayo Clinic 38% were of the large cell type 34% of the squamous cell variety and 16% of the small cell type the remaining 12% were adenocarcinomas Squamous cell carcinoma occurred 27 times more frequently in men than in women and small cell carcinoma was 29 times as frequent in men as it was in women In contrast adenocarcinoma and large cell carcinoma occurred respectively four and six times more frequently in men than in women

The various types of tumor also differ in their predilection as to the site of origin in the lung Small cell and squamous cell carcinomas tend to originate primarily in the large stem bronchi Adenocarcinoma tends to originate more frequently in peripheral bronchi whereas large cell carcinoma occurs about equally in the peripheral and in the central portions of the lung As might be anticipated the types of tumor is of significance in the ease of diagnosis

CYTOLOGY OF SPUTUM AND BRONCHIAL SECRETION

One of the most important and valuable aids in the diagnosis of carcinoma of the lung has been the development of a satisfactory method for the cytologic study of sputum and bronchial secretions for malignant cells Woolner and McDonald were able to make a positive diagnosis of carcinoma of the lung from cytologic study of sputum and bronchial secretions in 68% of routine cases of carcinoma of the lung A positive cytologic diagnosis of carcinoma of the lung can be made much more readily in cases in which the tumor originates from a large stem bronchus than in those in which it arises from a peripheral bronchus In small cell carcinoma and squamous cell carcinoma in which the tumor originates primarily in the large stem bronchi a positive cytologic diagnosis can be made in 93% of cases Conversely in adenocarcinoma which arises primarily in the peripheral bronchi a cytologic diagnosis can be made in only 48% of cases



Fig 25 Cavitating carcinoma of the lung

BRONCHOSCOPY

Bronchoscopy is of value in the study of carcinoma of the lung from the standpoint of diagnosis and also because it may assist in exact location of the tumor Although carcinoma of the bronchus usually presents a characteristic appearance as seen through the bronchoscope difficulty may be experienced at times in differentiating this lesion from adenomas tuberculomas or inflammatory lesions Consequently removal of tissue from the lesion for microscopic examination is imperative Negative results of bronchoscopic examination by no means rule out the possibility of a pulmonary tumor While the great majority of bronchogenic carcinomas arise from the large stem bronchi and should be visible readily during bronchoscopic examination some lesions are located in smaller stem bronchi that cannot be seen broncho

scopically or reached by means of biopsy forceps. The percentage of bronchogenic carcinomas that can be seen bronchoscopically and from which tissue can be removed for microscopic diagnosis depends on the type of lesion being examined. It is possible to make a positive bronchoscopic diagnosis in more than 80% of cases of small cell carcinoma of the lung. In contrast, a positive bronchoscopic diagnosis can be made in only about 28% of adenocarcinomas, which arise from the peripheral bronchi.

BIOPSY OF LYMPH NODES

The removal and microscopic examination of suspiciously firm lymph nodes from the supraclavicular region in patients who have indefinite pulmonary lesions always should be considered. Suspicious lymph nodes in the axilla or over the thoracic wall should be considered as suitable material for biopsy in unexplained pulmonary lesions. Occasionally, when all routine diagnostic measures have failed and palpable supraclavicular lymph nodes are absent, a lymph node containing malignant cells can be found in the anterior mediastinal space or in the retrosternal fat pad.

Thoracentesis and needle biopsy of the lung are other procedures that may be of value in the diagnosis of carcinoma of the lung.

In spite of all the diagnostic procedures available, a sizeable group of cases remains in which the only method of establishing the diagnosis is exploratory thoracotomy.

TREATMENT

The treatment of carcinoma of the lung is primarily surgical. Early and complete surgical eradication, as in carcinoma elsewhere in the body, is the procedure of choice. The results to be anticipated from surgical interference depend largely on the cellular type of the carcinoma. The most satisfactory results from surgical resection are obtained in adenocarcinoma and the squamous cell variety. Approximately 50% of patients with squamous cell carcinoma and 58% of patients with adenocarcinoma are suitable candidates for exploratory thoracotomy; resection can be accomplished in 60 to 70% of these patients. Following resection, 40% of patients who had squamous cell carcinoma and 54% of those who had adenocarcinoma will be living and well 5 years after operation. The results of surgical treatment of small cell and large cell carcinoma are much less favorable, and in small cell carcinoma especially it is imperative that some other form of therapy be seriously considered.

High voltage roentgen therapy or use of radioactive cobalt (Co^{60}) may be considered in cases in which the carcinoma is not resectable, or it may be given postoperatively when only palliative resection is done. Treatment of this form must be considered to be palliative.

Chemotherapeutic agents have been disappointing to the present time, but this form of treatment appears to hold the most promise for the future. Nitrogen mustard given intravenously has provided temporary benefit for many patients with nonresectable bronchogenic carcinomas. This is particularly true of the small cell variety. No claim for lengthening life can be made, but regression of symptoms and transient decrease in size of the lesions have been noted.

ALVEOLAR CELL TUMOR OF THE LUNG

Alveolar cell tumor of the lung is a distinct entity that is frequently confused with bronchogenic carcinoma. The literature abounds with speculation as to its relationship to jagziekte in sheep. The facts available at present do not allow a complete resolution of these problems. It is a comparatively rare tumor, being encountered in only 1 or 2% of all bronchogenic malignant tumors. It occurs slightly more frequently in men than in women (3:2). While it may occur at any age, it is much more frequently seen in the sixth decade of life. The tumor may involve varying segments of the lung. It may occur as a circumscribed

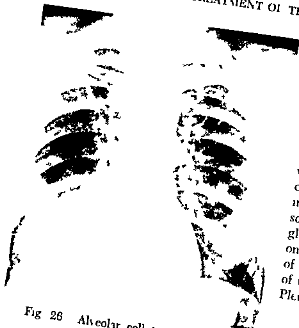


Fig 26 Alveolar cell tumor of lung

nodule or involve a complete lobe on occasion the entire lung may be affected Microscopically the alveolar septa are lined by nonciliated columnar cells Some cells contain mucus and pools of mucus may be present in the alveolar spaces Papillary projections into the alveolar spaces may be seen in some zones

SYMPTOMS

Cough is usually the earliest and most common symptom In most cases the cough is productive of a thin mucoid type of secretion that varies greatly in amount but is usually copious Hemoptysis may occur but is most likely a late manifestation of the disease Dyspnea is common occurring in about half the patients it is invariably constant and progressive once it develops Fever chills and loss of weight are other symptoms occasionally noted

The physical signs are dependent on the extent of the underlying pathologic condition but are of little value in attaining an accurate diagnosis

ROENTGENOLOGIC FEATURES

Although roentgenologic examination of the thorax has demonstrated a lesion in every case we have encountered there is nothing entirely characteristic about the roentgenologic findings (Fig 26) A poorly defined zone of consolidation having the appearance of ground glass usually is seen this may be localized to one part of the lung or associated spotty zones of infiltration may be present in other portions of the same lung or in the contralateral lung Pleural fluid is present in about 10% of cases

BRONCHOSCOPY AND CYTOLOGIC EXAMINATION

Bronchoscopy is of little direct value in the diagnosis of alveolar cell tumor of the lung In only one of 14 cases of alveolar cell tumor was it possible at bronchoscopy to obtain a specimen of tissue that on microscopic examination showed the tumor The presence of a copious frothy mucoid secretion coming from an involved segment of the bronchial tree should cause the endoscopist to suspect the possibility of alveolar cell tumor and to collect secretion for cytologic study

Cytologic examination of the sputum and bronchial secretions is an extremely valuable aid in the diagnosis of alveolar cell tumor In our experience a positive diagnosis can be established by this means in two out of three cases

TREATMENT

Surgical intervention is the method of treatment generally employed but so far the results have been far from satisfactory

BRONCHIAL ADENOMA

Bronchial adenoma is a tumor of a low degree of malignancy that arises from the mucous glands in the wall of the bronchus

Grossly these tumors vary greatly in size and appearance They generally project into the lumen of the bronchus and are attached to the

wall of the bronchus by a pedicle (Fig 27*a*) The pedicle may be long and narrow permitting free movement of the tumor in the bronchus or it may be short and the base of attachment broad (Fig 27*b*) Occasionally only a small portion of the adenoma may project into the lumen of the bronchus the remainder being situated in the bronchial wall and in the adjacent pulmonary tissue



Fig 27 Bronchial adenoma a Lesion with relatively narrow pedicle (hematoxylin and eosin x4) b Lesion with broad base of attachment (hematoxylin and eosin x3)

Adenoma of the bronchus may be divided into two types namely carcinoid and cylindroma The carcinoid type is more common approximately 90% of adenomas being of this variety Microscopically carcinoid adenomas can display some flexibility in their histologic pattern Vascularity of the tumor may be the dominant characteristic in this type the cells appear at times even to line the blood vessels At other times vascularity is much less pronounced The cells may form solid cords or may be grouped in alveolar clumps with acinar formation seldom a prominent feature

The histologic pattern of the cylindromatous adenoma also tends to vary somewhat and may be of two types One assumes a Swiss cheese pattern in which the irregular roundish and oval spaces are formed by the cells these spaces are filled with mucoid secretion The other is the tubercular pattern in which simple tubercles are formed

Although it is frequently stated that adenoma of the bronchus *occurs primarily in* young women our experience has not borne out this contention we have found approximately the same frequency in men as in women Although adenoma of the bronchus can occur at any period of life it tends to appear in younger persons than does carcinoma of the lung



Fig 28 Small adenoma of bronchus causing little generalized roentgenographic change in the lungs

The pulmonary symptoms produced by adenoma of the bronchus depend mainly on the location of the tumor its size and the degree of bronchial obstruction that it produces An adenoma of small size especially one located in the periphery of the lung that does not interfere with drainage of the bronchus or cause obstructive pneumonitis is likely to be asymptomatic (Fig 28) Lesions situated

closer to the hilus of the lung and that obstruct a large stem bronchus are much more likely to cause pulmonary symptoms (Fig 29) Cough is the most prevalent symptom being present in 85% of patients with adenoma Hemoptysis occurs in approximately half the patients Pain recurrent bouts of chills and fever dyspnea and respiratory wheeze are other symptoms frequently noted



Fig 29 Adenoma of bronchus with atelectasis and extensive roentgenograph c changes

The physical findings like the symptoms vary with the size of the tumor its location and the degree of bronchial obstruction Roentgenographic examination of the thorax may afford a definite clue to the identity of the lesion If the adenoma has reached sufficient size to cast a shadow it tends to produce one of two distinct roentgenologic patterns The more common is that which demonstrates evidence of obstruction of the airway of an entire lung a lobe or a pulmonary segment The less common form is characterized by a round or oval shadow on the roentgenogram

Bronchoscopy is of great value in the diagnosis of adenoma of the bronchus As seen through the bronchoscope the tumor presents a rather characteristic appearance (Fig 30) The tumor ordinarily is pedunculated and the mucous membrane that covers it is usually reddish yellow with small vessels coursing over the surface The mucous membrane seldom is ulcerated but pus usually exudes about the growth The tumor as a rule is firm and tends to bleed easily on manipulation Tissue should be removed from the tumor for microscopic examination in all cases Cytologic examination of sputum and bronchial secretions is of no value in the diagnosis of this lesion



Fig 30 Adenoma of the bronchus demonstrating how it would appear bronchoscopically

Opinion varies as to the most satisfactory treatment of bronchial adenoma The decision generally rests between removal or destruction of the tumor by bronchoscopic means and surgical extirpation of the tumor by bronchotomy lobectomy or pneumonectomy Varying with circumstances an adenoma that is pedunculated and attached to the bronchial wall by a narrow pedicle and is in such a location that its removal by means of thoracotomy would require pneumonectomy is best excised and removed through the bronchoscope Adenomas in people of advanced years or with physical ailments that would increase unduly the risk of thoracotomy are also better removed bronchoscopically All other adenomas are best treated by thoracotomy and complete surgical removal

BENIGN BRONCHIAL TUMORS

It is unusual for a tumor that is primary in a major bronchus to be anything but a carcinoma or an adenoma

Hamartomas are usually peripheral pulmonary tumors but occasionally they occur in a major bronchus, providing a bronchoscopic problem Approximately 32 such tumors in a major bronchus have been recorded in the literature It is believed that tumors formerly classified as chondromas, osteochondromas or lipochondromas probably would be classified as hamartomas by present criteria

Lipomas, lipofibromas, fibrolipomas and fibromas are closely related histologically and perhaps should be placed into one of only two groups, namely lipoma or fibroma, depending on the predominant tissue Lipomas occasionally extend through the bronchial wall and present both intrabronchial and extrabronchial portions in a dumbbell fashion

Tumor forming amyloid is found even less commonly than are the tumors already mentioned It is a localized collection of amorphous material giving the staining characteristics of amyloid It is not associated with generalized amyloidosis

The symptoms presented by patients having these tumors are those of other bronchial tumors Cough, hemoptysis, wheezing and pneumonitis must lead one to suspect the presence of bronchial obstruction

These tumors occasionally can be successfully removed bronchoscopically but more frequently they require surgical extirpation When the tumor occurs in a major bronchus, the surgeon should attempt transbronchial removal rather than pulmonary excision unless the portion of lung distal to the tumor is sufficiently diseased to warrant removal

BRONCHOLITHIASIS

Broncholithiasis has been recognized for many years Up to the time of the American Revolution, approximately 100 authors had described calculi or tophi that had been coughed up or found in the lung In spite of the long period of its recognition, it remains one of the most overlooked lesions of the bronchial tree

Broncholithiasis may develop in the tracheobronchial tree from a number of sources It may originate (1) in the lumen of the bronchus, as seen in the case of a long-retained aspirated foreign body, (2) in the bronchial wall, due to calcification of the bronchial cartilage, or (3) around the bronchus, with subsequent erosion through the wall of the bronchus Of these three sources, the most frequent is perforation of calcified tuberculous or anthracotic hilar lymph nodes into the tracheobronchial tree

Pollak, according to Kahler, in 1906 was probably the first to observe perforation of a tuberculous lymph node into the trachea Although the studies of Schwartz indicate that such tuberculous lymph nodes frequently erode into the bronchus, the erosion of calcified lymph nodes is much less common Sternberg, in a review of 6,132 cases of pulmonary tuberculosis in which necropsy was performed, noted 32 instances in which there was evidence of perforation into the tracheobronchial tree owing to anthracotic nodes

Broncholithiasis may occur at any period of life but, as might be anticipated, it is more likely to occur late in life than early In our experience at the Mayo Clinic, more than 70% of the patients were more than 40 years of age Broncholithiasis is encountered with equal frequency in men and women Broncholiths may occur in any part of the trachea or bronchial tree but, as might be expected because of the greater number of lymph nodes occurring adjacent to the right bronchial tree than to the left, a higher percentage of broncholiths will be found on the right side After the broncholith is extruded into the bronchial tree, it may be coughed from one side to the other

The syndrome of broncholithiasis is that of pulmonary suppurative disease The severity

of symptoms depends on the size and location of the broncholith. Perforation of the bronchus or trachea by a broncholith is usually accompanied by premonitory symptoms of cough, wheeze and dyspnea. The patient occasionally may expectorate a small calculus with no more than a mild cough. More frequently the cough is severe and protracted. With the perforation hemoptysis may occur and a paroxysm of coughing frequently obtains. If the perforating node is large it may produce alarming dyspnea that may terminate in asphyxia if the node is not removed promptly. Broncholiths vary considerably in size. Usually they are grayish white and irregular. They may show black zones of anthracosis. As a rule the perforating node is not large and after the initial paroxysm of coughing remains asymptomatic until secondary suppurative changes develop. Pieces may break off from the calcified broncholith and in turn cause other calcified deposits which may reach large numbers.

The possibility of a broncholith should be considered in any case in which the patient gives a history of pulmonary suppurative disease, especially if roentgenographic examination of the thorax reveals an abundance of calcareous material at the hilus (Fig. 31).

The bronchoscopic appearance in broncholithiasis varies with the stage of development of the broncholiths. If examination is performed before perforation of the node has occurred, one may see nothing abnormal or may notice an inward bulging of the tracheal or bronchial wall into the lumen corresponding to the underlying node. Less frequently one may have the good fortune to see a node just as it is about to perforate into the tracheobronchial lumen and to remove it. More frequently one may find the hole in a bronchus or trachea through which the node perforated and be able to pick out calcified material from the depths of the cavity. One or more broncholiths may be found loose in the tracheobronchial tree or embedded in a mass of granulation tissue.



Fig. 31. Broncholith in left main bronchus. Inset shows the calcified material after bronchoscopic removal.

The type of treatment depends on whether or not the broncholiths are loose in the tracheobronchial tree and whether or not they are causing symptoms. If the broncholith can be removed by endoscopic means this is the easiest and most satisfactory method of treatment. If it cannot be removed by endoscopy and is causing pulmonary symptoms, lobectomy or even pneumonectomy may be required.

BRONCHOSTENOSIS

Bronchial obstruction may be due to a great many causes. It may be complete or incomplete, constant or intermittent. For an understanding of the mechanics of bronchial obstruction it must be appreciated that the bronchial tree is not a system of rigid tubes. The lumen of each bronchus widens and lengthens with inspiration and it narrows and shortens with expiration; this rhythmic change in bronchial diameter allows certain lesions to obstruct the bronchus more nearly completely during expiration than during inspiration.

In the present discussion bronchial obstruction due to a foreign body, benign or malignant tumors or tuberculosis will not be con

sidered Ephraim, Mann, von Schrötter and others called attention to the fact that swelling of the mucous membrane may take place in chronic bronchitis, which in turn may lead to obstruction of a bronchus of small caliber Such obstruction is most likely to occur in a secondary or tertiary bronchus Bronchostenosis characteristically causes repeated attacks of chills, fever, cough and the "sputum retention" syndrome, in which symptoms clear rapidly when the patient succeeds in expectorating the infected retained secretion Obstruction of the bronchus due to swelling of this type usually lasts 3 to 5 days Patients may become so accustomed to their symptoms that they are unaware of them and pay no heed to the underlying cause

The episodes of chills and fever may occur at various intervals and often may be mistaken for attacks of pneumonia, malaria or rheumatic fever Physical and roentgenographic examinations between such attacks may reveal no abnormalities, but during an episode of fever and cough they may give evidence of consolidation of the segment or lobe distal to the obstruction If the narrowed bronchus can be found and the bronchus adequately dilated, the patient's symptoms will promptly subside However, the dilation may have to be repeated at various intervals, as stenosis may recur

ATELECTASIS

Atelectasis is a complicated phenomenon, and considerable controversy over definition of the term has taken place Although according to Gairdner, Louis first distinguished pneumonia from atelectasis in 1829, it was not until 1890, with Pasteur's description of massive atelectasis, that the attention of the medical profession was attracted to this condition Many theories have been advanced to account for the development of atelectasis

For clinical purposes, Adamson has offered a useful classification of the types of atelectasis as follows (1) congenital atelectasis with bronchial atresia, or agenesis of alveoli with interference in aeration of small or large portions of the lung, (2) adjustment atelectasis, which represents a decrease in the volume of the lung occasioned by pleural effusion, paralysis of respiratory muscles, and other factors that decrease the effective intrathoracic space, (3) obstructive atelectasis, which results from bronchial occlusion

The third type is of chief practical importance It is classified into two subgroups, namely that occurring after an operative procedure and that due to other causes It is said to occur in 10% of operations performed on the thorax or upper part of the abdomen

The sequence of events in postoperative atelectasis and in massive atelectasis of non surgical origin is as follows As a result of shock, suppressed cough reflex and dehydration, thick tenacious secretion is formed and may plug the bronchial tree As a rule, most patients who aspirate material into the lung while under anesthesia are able to rid themselves of this material on recovering consciousness, through either the cough reflex or ciliary action If the material is not expelled, however, and is permitted to remain in the bronchus, it soon leads to atelectasis of the portion of the lung beyond the point of bronchial obstruction

The syndrome associated with atelectasis follows a rather definite pattern The patient usually complains of dyspnea that is frequently out of proportion to the degree of pulmonary involvement, and also of a sense of discomfort over the thorax corresponding to the involved lung The pulse accelerates and the temperature suddenly increases Cyanosis is often present, its degree depending on the amount of tissue involved In massive atelectasis, the heart and mediastinal structures shift toward the side of involvement and the respiratory excursion on the affected side decreases Postoperative atelectasis itself is not primarily a suppurative process, but secondary infection may develop readily if it is permitted to persist

Bronchoscopy is of the greatest value not only in the treatment of all types of atelectasis



Fig 32 a Massive atelectasis b The day after bronchoscopic aspiration

but also in the prevention of postoperative atelectasis for this condition can be largely prevented by eliminating the factors that give rise to its development No patient should be permitted to leave the operating table with a so called wet lung Most patients who have postoperative atelectasis are able to overcome the difficulty simply by rolling over on the uninvolved side and coughing up the retained secretion In certain cases however this procedure does not suffice and more drastic measures must be employed Bronchoscopy can be of great value In the early stages a tenacious plug usually can be seen at the time of bronchoscopy and can be aspirated with prompt subsidence of the zone of atelectasis (Fig 32) If atelectasis has persisted for an appreciable period the plug of mucus may have undergone resolution and the bronchus will be filled with mucopurulent or even serous material As much as 300 to 500 ml of this material often can be aspirated from the bronchus with pronounced improvement in the patient s condition

BRONCHIAL OBSTRUCTION BY COMPRESSION

Compression of the trachea or bronchi may be produced by structures in apposition to the airway It is almost impossible to distinguish the clinical symptoms and signs produced by such obstruction from those caused by intrabronchial and intratracheal obstruction

The trachea is susceptible to compression by such lesions as vascular anomalies intrathoracic thyroidal adenomas mediastinal tumors and cysts bronchial cysts and metastatic deposits in lymph nodes The bronchi also can be compressed by similar lesions along with such entities as thymic tumors or lymphosarcoma Enlarged peribronchial lymph nodes may cause bronchial compression (Fig 33) Although such obstruction may be encountered in any pulmonary lobe the bronchus of the middle lobe on the right is especially prone to such occlusion by enlarged lymph nodes As a result of such obstruction the lobe decreases in size and becomes consolidated with dilatation of the bronchi there may be evidence of suppuration depending on the duration of obstruction This change when present in the middle lobe is often described as the middle lobe syndrome" (Fig 34) Obstructive pneumonitis with bronchiectasis may occur in any part of the lung

Roentgenologic examination of the thorax especially tomography may reveal the exact location of an obstruction of the bronchus Bronchography also may be of value in this respect Unfortunately it does not indicate the exact nature of the causative lesion Al



Fig. 33. Compression of lower end of trachea by a calcified lymph node. a, Anteroposterior view. b, Tomogram.

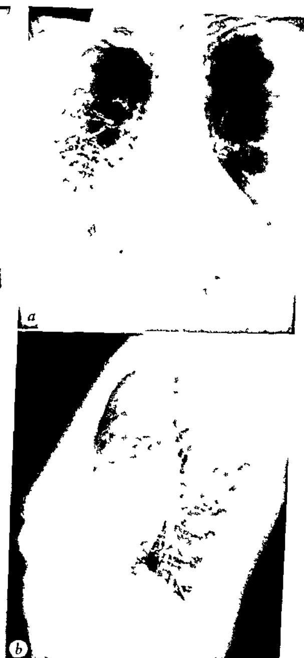


Fig. 34. Bronchographic appearance in middle-lobe syndrome caused by a broncholith. a, Anterior view. b, Lateral view.

though bronchoscopy may demonstrate the site of obstruction and on occasion furnish a clue as to its possible cause, this is the exception rather than the rule.

When indicated, surgical resection of the segment of the lung affected by the obstruction is usually curative. On occasion, at operation and on pathologic study, an obstructing lesion cannot be identified because it either has eroded into the bronchus or has undergone retrogression, leaving only the residue of the damage produced. When compression is caused by enlargement of the thyroid gland or a thymoma, the tumor may be successfully

resected The collapse of the trachea that occurs after removal of an adenomatous goiter that has compressed the trachea may be obviated at times by insertion of a bronchoscope or tracheotomy tube into the trachea Collapse of the trachea following thyroidectomy may be permanent Carcinoma of the thyroid occasionally perforates into the trachea and causes respiratory symptoms it may be possible in such cases to obtain tissue from the trachea at the time of bronchoscopic examination and establish the correct diagnosis

BRONCHO-ESOPHAGEAL AND TRACHEO-ESOPHAGEAL FISTULAS

Tracheo esophageal and broncho esophageal fistulas are comparatively rare conditions that may be congenital or acquired in origin Congenital fistulas generally are associated with esophageal atresia if allowed to persist they rapidly give rise to pulmonary suppuration and death Much progress has been made in recent years in their early diagnosis and



Fig 35 Broncho esophageal fistula

definite advancements have been made in their successful surgical closure One variety of congenital broncho-esophageal fistula exists that is not associated with esophageal atresia and is compatible with life In this type the opening between the esophagus and bronchus is of such a size and position that solid foods especially do not readily gain access to the bronchus (Fig 35) While liquids can and do pass through the fistula the patient soon le rns to ... the bronchus It is surprising how the bronchial tree in such cases accommodates itself to the irritation from the offending liquids and solids

Acquired tracheo esophageal and broncho esophageal fistulas may be due to a great variety of conditions Carcinoma of the esophagus usually terminal in nature is the commonest cause of such lesions Foreign bodies in the esophagus may cause a fistula between the esophagus and the tracheobronchial tree The removal of such a foreign body often is followed by spontaneous closure of the fistulous tract. Fistulas resulting from trauma are usually amenable to surgical intervention Syphilitic fistulas are best treated by measures directed toward the syphilitic infection and often will close without further treatment Fistulas secondary to traction diverticula usually do not appear until after the second decade of life for traction diverticula of the esophagus do not manifest themselves until after this age In a fistula associated with traction diverticula a calcified node or nodes invariably will be found along the course of the fistulous tract and must be removed at the time of operation if the fistula is to be closed successfully Fungous disease such as actinomycosis may produce broncho-esophageal fistulas The local application of caustics to the fistulous tract seldom brings about closure

The differential diagnosis between tracheo esophageal fistula and bulbar palsy at times may offer considerable difficulty Esophagoscopy bronchoscopy and studies of esophageal motility along with roentgenographic examination may be necessary to allow a correct diagnosis

ASTHMA

The present discussion will not encompass the entire problem of bronchial asthma but will be limited to the role of bronchoscopy in dealing with the situation Bronchoscopy has been recognized for a long time as of value in the treatment of asthma Pieniazek, in 1905, was probably the first to carry out an endoscopic examination on a patient during the course of an asthmatic attack He found that the bronchi were greatly congested, with considerable stenosis of the smaller bronchi during the period of attack These findings subsequently have been confirmed frequently by other observers The bronchi often are filled with a tenacious gelatinous secretion In the intervals between attacks of asthma, the bronchial mucous membrane may appear perfectly normal In many cases, however, residual evidence of bronchitis will be found

Since Pieniazek's report, many writers have pointed out that good results may be obtained in the treatment of asthma by bronchoscopic aspiration The simple process of aspirating secretion from the bronchus may result in improvement in the condition, but as a rule improvement is only temporary

An important complication of either allergic or infectious asthma is bronchostenosis This bronchostenosis is inflammatory in origin and is not referable to allergic edema or bronchial asthma Two outstanding disturbances of function result when a bronchus becomes stenosed, namely (1) movement of air entering or leaving the pulmonary tissues beyond the region of stenosis is inhibited, and (2) bronchial secretions, which usually are excessive in asthma, are retained below the stenotic zone so that a region of partial or complete atelectasis results The possibility of bronchostenosis should be entertained in any asthmatic patient who has had attacks in which the cough becomes nonproductive and is associated with febrile episodes either with or without preceding chills. As a rule, the fever lasts 2 to 5 days With subsidence of fever, the amount of sputum usually increases It should be emphasized that febrile episodes, hemoptysis or purulent sputum do not accompany uncomplicated asthma

Bronchoscopic examination may disclose one or more stenotic bronchi The superior branches of the bronchi to the lower lobes are involved most frequently The stenotic bronchus is dilated carefully, after which a small amount of purulent secretion usually can be aspirated When bronchostenosis is present and the stenotic bronchus is dilated adequately, the patient usually experiences prompt improvement of the asthma Recurrence of bronchostenosis may take place, in such instances, further bronchoscopic dilation of the stenotic zone is indicated

SYPHILIS OF THE TRACHEOBRONCHIAL TREE

Syphilis of the tracheobronchial tree is extremely rare at present It tends to assume one of two types, namely (1) lesion of gummatous infiltrative nature, and (2) lesions that are produced by secondary cicatricial stricture No characteristic symptoms are ascribable to the disease A diagnosis of syphilis based only on positive results of serologic tests does not always signify that a lesion involving the tracheobronchial tree is of syphilitic origin While microscopic examination of tissue removed from the lesion may be suggestive of syphilis, the final diagnosis often depends on the response of the lesion to antisyphilitic therapy

HEMOPTYSIS

Bronchoscopy is indicated in any case of unexplained hemoptysis Such a statement assumes that tuberculosis, pneumonia, aneurysm or cardiac decompensation has been excluded as an etiologic factor Some difference of opinion exists as to how soon after pulmonary hemorrhage bronchoscopy should be performed Myerson recommended that at

least 10 days should elapse between the hemorrhage and bronchoscopy We agree with Arbuckle that it is safe, and the best results are obtained, if the examination is done as soon as possible after the bleeding has subsided It is thus possible, by tracing the blood in the bronchial tree, to determine more easily from which bronchus the bleeding is arising and also the cause of the hemorrhage When results of bronchoscopic examination are negative, bilateral bronchography should be performed

Among the more common causes of hemoptysis are tuberculosis carcinoma mitral stenosis benign tumor bronchiectasis pulmonary abscess broncholithiasis, foreign body acute tracheobronchitis such as follows inhalation of various irritating gases and diffuse polypoid laryngotracheobronchitis The opinion most frequently reached in cases in which the source of gross hemorrhage is not readily apparent is that the bleeding must be due to varices It has been our experience that such varices are rare and that the bleeding usually comes from some other source Gerlings reported three cases of hemoptysis due to venous stasis of the trachea in which treatment by cautery was used A great difference exists in the tendency of mucous membranes to bleed It is not possible in some cases to determine definitely the cause of bleeding which appears to be diapedesis This condition often is associated with hypertension

Various methods of treatment have been advocated for pulmonary bleeding of indeterminate origin among which may be mentioned the use of venom from the moccasin snake Beneficial results sometimes may be obtained according to Vinson in cases of unexplained pulmonary hemorrhage such as in diffuse tracheobronchitis by curettage of the involved bronchus followed by insufflation of powdered sulfanilamide When the bleeding is attributable to other causes the hemorrhage may be controlled at times by local application of cocaine and epinephrine, as well as by local pressure with a tampon at the site of bleeding The local application of a small amount of fer de lance venom to the site of bleeding may adequately control the hemorrhage

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CHAPTER 7

Pneumonia

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INTRODUCTION

PNEUMONIA IN GENERAL

GREAT ADVANCES in knowledge were made in the field of acute infections of the respiratory tract in the past two decades. After the adoption of the etiologic mode of diagnosis and classification, many "new" specific entities emerged from the large group of previously undifferentiated major and minor pulmonary infections. Antimicrobic therapy brought about great changes in the clinical aspects of several bacterial pneumonias and reduced their mortality rate (Fig. 1). Physicians who entered practice after 1940 have views on pneumonia as different from those of the preceding generation as that generation had on typhoid as compared with their forebears.

Of the newly recognized forms, pneumonias of viral origin associated with a number of minor infections of the respiratory tract are the most common and outnumber those caused by bacteria. They had always existed but were obscured by interest in the more fatal bacterial pneumonias. Mycotic pneumonias once were regarded as rarities, but pulmonary involvement is the chief manifestation of histoplasmosis and coccidioidomycosis, and its clinical resemblance to other pneumonias delayed its recognition. The same can be said for Q fever and psittacosis.

Some of the newly classified pneumonias are primary infections of the lung; others like those caused by brucellas or rickettsias are pulmonary manifestations of systemic disease. The lungs may be involved in sarcoidosis, disseminated lupus erythematosus and polyarteritis. Pneumonias may be caused by mechanical, chemical or physical means. Secondary pneumonias are those in which the lungs, injured by other causes, are invaded by bacteria ordinarily present in the respiratory tract. These occur as a result of atelectasis, stasis, foreign bodies, tumors and other factors, and usually are associated with a mixture of bacteria. Over 50 kinds of pneumonia are now classified etiologically, but many of them seldom are encountered (Table I).

INCIDENCE

Statistics of the incidence of pneumonias generally are incomplete. The number of cases of different kinds varies from year to year and from place to place, depending on the prevalence of the causative agents and other factors. Many diagnoses are faulty. There are no statistics on the large number of acute pulmonary infections secondary to other disease or of hypostatic, atelectatic and terminal pneumonia. Viral pneumonia is not a "reportable" disease and rarely is included in statistics. If, as estimated, 20 000 000 persons in the United States are infected with H. capsulatum, histoplasmic pneumonia is a frequently unrecognized, unreported disease.

According to tabulation by Dingle in 1953 the relative incidence of pneumonia as com

With the exception of Figure 9, all illustrations are reproduced from Reimann: *Pneumonias* (Springfield: Thomas, 1971).

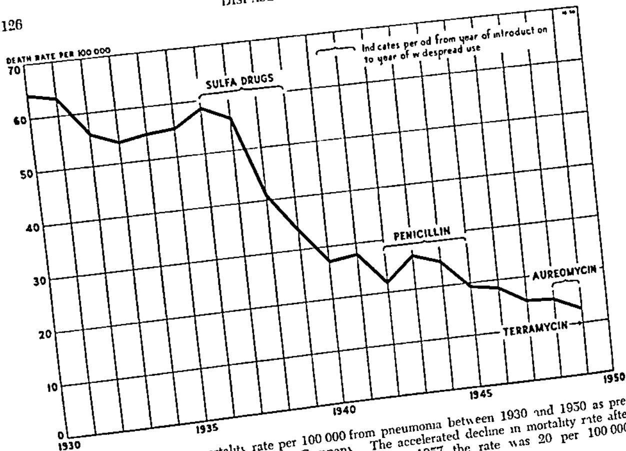


Fig 1 Curve of the mortality rate per 100 000 from pneumonia between 1930 and 1950 as prepared by the Metropolitan Life Insurance Company The accelerated decline in mortality rate after the introduction of antimicrobic therapy began in 1937 In 1957 the rate was 20 per 100 000 (From Reimann *Pneumonia* Springfield Thomas 1954)

pared with infections of the upper part of the respiratory tract is about as shown in Table II

The percentages shown fluctuate from year to year according to the epidemic prevalence of any of the infections Viral infections of the respiratory tract obviously far exceed those of bacterial origin Pneumococcic lobar pneumonia it may be noted is and always was an uncommon disease Even in the past the average practitioner seldom dealt with more than 1 or 2 cases a year Its striking clinical behavior its dangerous complications and its high mortality rate left lasting but exaggerated impressions of its incidence

Other reasons for statistical distortion may be cited Most studies and statistics of pneumonia emanate from hospitals where severely sick patients are sent At present perhaps most patients with pneumococcic pneumonia are cured with antimicrobic drugs at home and their cases escape inclusion in statistical reports Furthermore the deplorable indiscriminate use of antimicrobics for trivial respiratory tract infections no doubt has had some good effect at times in curing bacterial pneumonias in their earliest stage before diagnosis is possible Bacterial pneumonia however develops in less than 0 1 or 0 2% of patients with viral infections of the upper respiratory tract There is little reason to believe that the actual incidence of bacterial pneumonias has lessened Resistance to infection is unchanged predisposing viral infections have not been controlled specific prophylaxis is impracticable or unsuccessful and microbes are as invasive and pathogenic as ever

The pneumococcus is the most important bacterial cause of primary pneumonia as shown by statistics gathered in Table III by Dowling

Except in small epidemics bacterial pneumonias other than pneumococcic ones are rare diseases

TABLE I

LIST OF CAUSES OF PNEUMONIA

I—Specific Forms of Pneumonia	*II—Diseases Accompanied by Specific Pneumonia*	*III—*	*IV—Pneumonias not Caused by Infections*
Cocci	Tularemia	Pneumonia caused by	Oil aspiration
D. pneumoniae	Plague	specific infectious agents	Radiation
Streptococcus pyogenes	*Brucellosis*	*or mixed infection sec-*	*Chemicals*
Staphylococcus aureus	Glanders	ondary to acute and	Allergy
G. tetragena	Diphtheria	chronic diseases shock,	Bagasse
N. meningitidis	Typhoid	mechanical causes,	Byssinosis
N. catarrhalis	Colon bacillus infection	trauma senility, etc	*Uremia*
others	Bacillary dysentery		In sarcoidosis
Bacillary	Rheumatic Fever		In collagen diseases
H. influenzae	Syphilis		
H. pertussis			
Kl. pneumoniae	Scrub typhus		
Ps. aeruginosa	Epidemic typhus		
M. tuberculosis	Rocky Mountain spotted		
P. tularensis	fever		
B. anthracis	Infectious mononucleosis		
P. pestis	Erythema multiforme		
Salmonella	exudativum		
others			
Viral			
Adenoviruses			
Influenza	*Malaria*		
Measles	Amebiasis		
Variola	Leishmaniasis		
Vaccinia	Toxoplasmosis		
Varicella	Ascariasis		
Lymphocytic chorio-	Strongyloidiasis		
meningitis	Schistosomiasis		
Salivary gland virus	Ankylostomiasis		
Unknown (Viral pneu-	Trichiniasis		
monia)	Paragonimiasis		
Psittacosis-ornithosis	others		
lymphogranuloma			
Coxiella burneti			
Fungal			
Coccidioides immitis			
Histoplasma capsulatum			
Candida albicans			
(monilia)			
Crypt. hominis (torula)			
Actinomyces			
Nocardia			
others			
Tyroglyphus tarsonemus			
Pneumocystis carinii			

MORTALITY

General mortality statistics are more reliable than ones of incidence. Yet many diagnoses are erroneous or are reported as pneumonia when pneumonia is not present. Terminal pneumonias often are included even though pneumonia was not the primary cause of

TABLE II

Undifferentiated upper respiratory tract disease (colds, grip, etc.)	94.8%
Hemolytic streptococcic sore throat	2.4%
Nonstreptococcic (viral) pharyngitis	1.6%
Viral pneumonia	0.7%
Influenza	0.4%
Pneumococcic pneumonia	0.1%

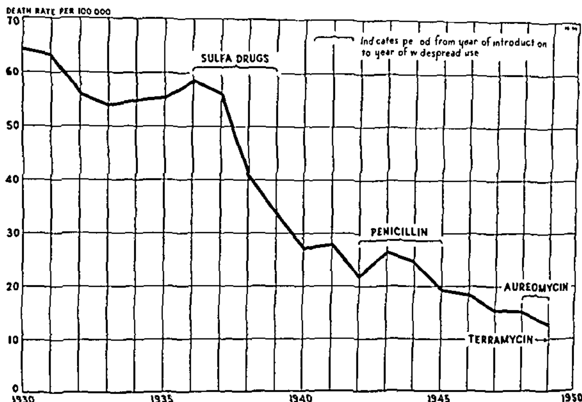


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H pertussis			
Kl pneumoniae	Scrub typhus		
Ps aeruginosa	Epidemic typhus		
M tuberculosis	Rocky Mountain spotted fever		
P tularensis			
B anthracis	Infectious mononucleosis		
P pestis	Erythema multiforme exudativum		
Salmonella			
others			
Viral			
Adenoviruses			
Influenza	Malaria		
Measles	Amebiasis		
Variola	Leishmaniasis		
Vaccinia	Toxoplasmosis		
Varicella	Ascariasis		
Lymphocytic choriomeningitis	Strongyloidiasis		
	Schistosomiasis		
Salivary gland virus	Ankylostomiasis		
Unknown ("Viral" pneumonia)	Trichiniasis		
	Paragonimiasis		
Psittacosis-ornithosis lymphogranuloma	others		
Coxiella burneti			
Fungal			
Coccidioides immitis			
Histoplasma capsulatum			
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TABLE III

D. pneumoniae	98.1%
Streptococcus hemolyticus	0.9
Kl. pneumoniae (Friedländer's bacillus)	0.6%
H. influenzae	0.3%
Staphylococcus	0.1%

death but developed because the patient was dying *from some other cause*.

Before the antimicrobic era 1 of every 3 or 4 victims of pneumococcic pneumonia died; many developed empyema with prolonged illness and the results of complex serotherapy left much to be desired. Antimicrobic therapy reduced the gross death rate of pneumococcic *pneumonia to less than 10%*. It also is effective in saving life in tularemic and plague *pneumonia*, but less so in the *entities* caused by other bacteria listed in Table III.

Pneumonia was *the third most important* cause of death in the United States before 1940. Now it ranks sixth or seventh. According to statistics from a life insurance company the mortality from pneumonia among policyholders has declined 85%.[1] Lest this striking gain give a false sense of security, it must be emphasized that pneumonia still causes over 50,000 deaths annually in the United States. The mortality rate stays high at the extremes of life: 24% of deaths from pneumonia are in premature and very young infants and 46% are in persons over the age of 65. Pneumonia will be a major cause of death for some time to come.

Problems of prevention and treatment are *far from settled*. *Antimicrobic* therapy may have reached the limit of success. Other measures to prevent both viral and bacterial infections, and to improve general resistance of the *host are needed* if greater success is to be achieved, especially at the extremes of life. It is likely that the former high mortality rate of bacterial pneumonias will return should some unforeseen catastrophe stop the manufacture, distribution or use of antimicrobic drugs.

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THE VIRAL PNEUMONIAS

Nonbacterial Pneumonias, Primary Atypical Pneumonia

Filtrable viruses were known to cause inflammation of the lungs for decades, yet little attention was aroused in the matter. It has *taken many years to learn that viruses are the* most frequent causes of pulmonary infection. Pneumonia may be incidental to systemic viral diseases like measles, or more often it is a *primary infection of the respiratory tract*. In the latter sense viral pneumonias were brought to general attention in 1938 by Reimann.[1] The term Viral pneumonia was introduced *at that time* because all evidence except the isolation of a virus pointed to *one or more of them* is the cause. Unfortunately the cumbersome name "primary atypical *pneumonia of unknown etiology*" was applied officially. Viral pneumonia, however, is typical of itself and atypical only if compared clinically with lobar pneumonia as the arbitrary *prototype*.[2] Further confusion arose since some observers regard viral *pneumonias* as complications of minor upper respiratory tract infections or as separate coincidental infections. This view probably is influenced by *memory of the severe bacterial pneumonias* which complicated influenza in the pandemic of 1918 and by the fact that lobar pneumonia often is preceded by "colds." It is more likely that most viral pneumonias are the severest forms of a number of minor viral infections of the upper respiratory tract as indicated schematically in Figure 2.

Primary viral pneumonias for the most part are components of influenza, colds, adenoviral disease, viral pharyngitis, and of entities still to be delineated.[3] There also are kinds of unknown cause which occur sporadically and in small localized epidemics in the absence of coincident overt cases of mild nonpneumonic disease.[4] A segment of the problem was clarified by the discovery of influenza viruses after 1933 and of a number of adeno-

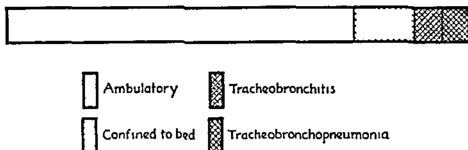


Fig 2 Schematic representation of an epidemic of acute viral respiratory tract infection in an institution About half of 800 persons remained well About 400 were affected in graded degrees of severity as illustrated by the bar Of these 75% were slightly sick but ambulatory 25% were bedridden 12% had tracheobronchitis and 6% had pneumonia (From *Arch Int Med* 65 141 1940)

viruses after 1952 These viruses have been isolated from patients with either mild disease or pneumonic attacks Evidence of their pathogenic activity can be detected by serologic methods

ETIOLOGY

Adenoviruses are grouped into 14 serotypes Types 3 4 and 7 were recovered from patients with upper respiratory tract diseases and from some with pneumonia Volunteers inoculated with these viruses developed mild disease and a few had pneumonia Cold agglutination of erythrocytes did not occur Another virus called PAP was recovered from patients in whose blood cold agglutinin and agglutinin for streptococcus MG did appear Viral pneumonias and their basic diseases are caused by a number of filtrable agents some of which still are undiscovered Influenza viral pneumonia is discussed on page 134

EPIDEMIOLOGY

The epidemiology of each entity varies according to the prevalence and dissemination of its causative virus In general viral pneumonias are infectious and contagious air borne diseases Their source is the patient or a healthy carrier of the virus Transmission by other means may occur Viral pneumonia is usually appear during epidemics of mild respiratory tract diseases Another form occurs sporadically or in small localized outbreaks unaccompanied by mild cases and behaves epidemiologically like psittacosis

INCIDENCE

The curve of incidence of viral pneumonias coincides with that of their basic minor respiratory tract infections of which they are the severe forms It is highest in the cold months but summer outbreaks and sporadic cases occur No large epidemics have been reported since 1942 During epidemics in certain communities viral pneumonias had an incidence rate of 14 to 35% and constituted 70% of all pneumonias Endemically they accounted for 1 or 2 cases per 1 000 per week

PATHOLOGY

The disease rarely is fatal and few reports of necropsy studies are available The mucous membrane of the greater part of the respiratory tract may be inflamed and dry but in some cases the lungs almost alone are affected There are discrete or confluent soft greyish pink or red patches areas of atelectasis and emphysema A small amount of exudate is found in the bronchi Microscopically there is interstitial involvement The alveolar septums are invaded with mononuclear cells The alveoli are filled with a serous exudate red cells and leukocytes predominantly of the mononuclear form A hyaline membrane lines the alveoli occasionally In a form of viral pneumonia in infants cytoplasmic inclusion

bodies are present in cells lining the inflamed respiratory tract

CLINICAL

The clinical behavior of most pneumonias caused by filtrable viruses and of the pneumonias presumably viral in origin is remarkably similar and constant except that all gradations from mild to severe disease occur

The onset may be sudden with a chill or chilliness but it often is gradual merging with previous discomfort and inflammation of the upper respiratory passages Coryza and rhinorrhea may occur A dry "scratchy" or slightly sore throat and conjunctival irritation are common complaints in the beginning The temperature rises gradually or rapidly and with it appear headache general aching anorexia hoarseness and dry paroxysmal cough In mild cases few other symptoms occur and recovery follows after 2 or 3 days or more Many patients are ambulatory and pneumonia passes unrecognized Roentgenograms usually show transient intensification of the hilar shadows and small or large localized or scattered areas of pulmonary infiltration

In severe cases fever may rise to 104°F (40°C) or more during the first week (Fig 3) Headache drowsiness and photophobia may be intense and may suggest encephalitis Chilliness with profuse sweating may occur and recur They are distressing features Paroxysmal cough with little or no sputum often is caused by a change of position Pleurisy is uncommon The clinical course may resemble typhoid or psittacosis (Figs 4 and 5) The spleen occasionally is palpable There often is relative bradycardia in the early stage and the respiratory rate may not be increased Cyanosis is common

Suppressed breath sounds and rales may be heard early in a localized area but a striking feature is the absence or paucity of abnormal signs and the surprize on finding large areas of infiltration by roentgenography Later dulness increases the breath sounds may be suppressed or weakly bronchial and rales persist Signs of frank consolidation do not occur The lesion may be localized but it often

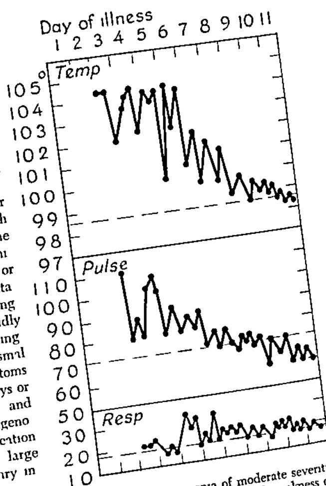


Fig 3 Viral pneumonia of moderate severity A man aged 38 noticed aching and weakness on January 14 but continued to work In the evening a chill occurred followed by fever and cough productive of a small amount of brown sputum In the next two days there were repeated chills profuse sweating occasional cough and scant sputum Because of his symptoms high fever and relative bradycardia his physician suspected typhoid administered streptomycin and sent him to the hospital On examination he was flushed and dry The conjunctivas nasal and pharyngeal mucosa were reddened Cough was harassing Rales and roentgenographic density were present in the right middle lobe The leukocytes numbered 15 000 Culture of the sputum revealed the usual flora and blood culture was sterile The pharyngeal exudate was composed chiefly of mononuclear cells Cyanosis and dyspnea required therapeutic oxygen By the fifth day the pneumonic process had involved the whole right lung Sweating and bradycardia persisted Cold agglutination did not occur and a complement fixation test for psittacosis during convalescence was negative Fever gradually declined and became normal on the eleventh day (From Reimann *Pneumonia* Springfield Thomas 1954)

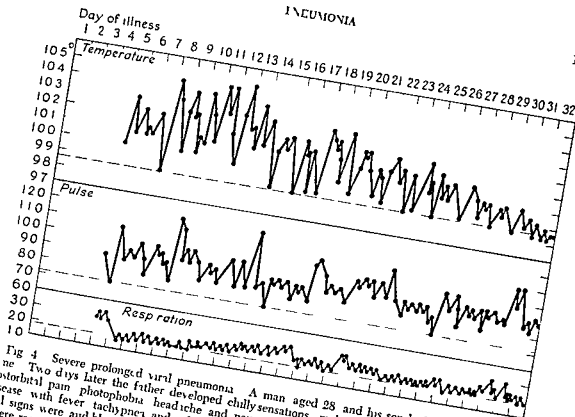


Fig 4 Severe prolonged viral pneumonia A man aged 28 and his son had colds at the same time Two days later the father developed chilly sensations malaise fever and profuse sweating postorbital pain photophobia headache and nausea He entered the hospital on the fourth day of disease with fever tachypnea and relative bradycardia The pharynx was reddened but no abnormal signs were audible in the lungs About the ninth day rales were audible in the right base where roentgenographic density was visible The leukocytes varied between 5 000 and 7 000 Tuberculosis and typhoid were suspected but appropriate tests were unrevealing Because the patient had lived in a region where coccidioidomycosis and Q fever were endemic these diseases were suspected but ruled out By exclusion a diagnosis of viral pneumonia was made Cold agglutination did not occur Bradycardia persisted and the fever disappeared on the thirty second day of disease (From Reimann *Pneumonia* Springfield Thomas 1954)

spreads from one area to another and to the other lung until in some cases all of the lobes are involved in turn or all at once The severity of the disease may not be in proportion to the extent of the lesion In certain severe cases during an epidemic there may be minimal or no invasion of the lung suggesting that certain varieties of viral pneumonia are incidental to a systemic disease In other cases there may be extensive lesions in the lung with only moderate or mild illness

Complications and *sequels* are rare The most important is a shocklike state or circulatory collapse with pulmonary edema which is the chief cause of death Considerable weight may be lost and convalescence may be slow Relapse or recurrence may follow Superinvasion of bacteria rarely occurs but must be considered if evidence of it appears or if antimicrobic therapy is inadvertently applied Hemolytic crisis has been observed in patients treated with sulfonamide drugs Pleurisy and pericarditis seldom occur Meningomyelitis and encephalitis have been reported Pulmonary fibrosis emphysema and bronchiectasis have been feared but are rare as sequels These conditions in unrecognized form may antedate pneumonia

PROGNOSIS

Viral pneumonias last from a few days to several weeks (Figs 4 and 5) There is no acceptable evidence that antimicrobic therapy influences the course The fever ends by lysis Roentgenographic shadows disappear slowly

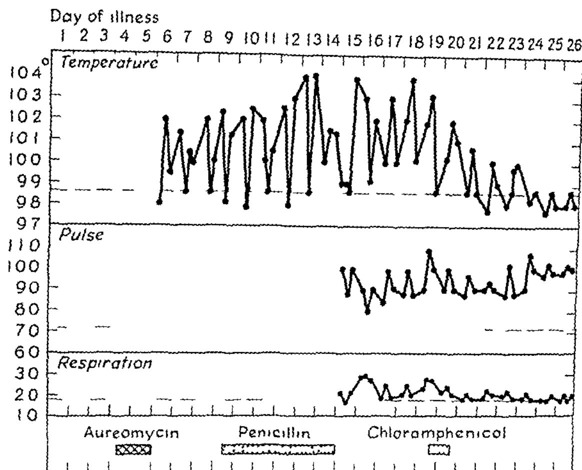


Fig. 5 Severe sporadic viral pneumonia. A woman aged 66 coughed for about 10 days until on November 12 two chills occurred. Cough intensified and profuse sweating and chilliness recurred. Headache was severe. Aureomycin administered by her physician caused diarrhea and had to be stopped. Penicillin was given but because the condition became worse she entered the hospital on the fifteenth day. Relative bradycardia was present and the leukocytes numbered 4 000. Because the patient had eaten raw oysters in early November typhoid was suspected. Chloramphenicol given for two days had to be stopped because of severe diarrhea. All cultural and serologic studies were negative as were tests for Q fever and psittacosis. Rales and roentgenographic densities were prese[illegible] injected. On [illegible] and the patie[illegible] Springfield Thomas 1954)

and completely but sometimes persist for weeks. Most of the deaths occur in patients with other chronic disease, from bacterial invasion or from circulatory failure. The death rate is less than 1%.

LABORATORY STUDIES

The number of blood leukocytes usually is normal or slightly diminished but may be increased later. The sedimentation rate of red cells is increased somewhat especially late in the disease. The sputum often is scanty, rarely blood tinged and contains bacteria usually found in the oropharynx. Many monocytes may be in the sputum and in scrapings from inflamed mucosa. Cold agglutination of erythrocytes or agglutinin for streptococcus MG appear in the blood in about 50% of cases in some epidemics, in most cases and in others in none. To be of diagnostic import the titers should be measured on successive occasions and show a rise over 1:32 during or after the second week of disease.

Adenoviruses can be isolated by special tissue culture or other methods. Routine diagnosis can be made by the complement fixation test and the type of adenovirus determined by the specific neutralization test.

DIAGNOSIS

Early diagnosis may be made clinically, especially during an epidemic. It is aided by appropriate laboratory tests, roentgenography, and by ruling out pneumonias of known cause. A normal or nearly normal leukocyte count, a slightly increased sedimentation rate, an absence of pathogenic bacteria in scanty sputum and a sterile blood culture are important features. Unfortunately, significant titers of cold agglutinin for erythrocytes and agglutinin for streptococcus MG appear in only 50% of cases and too late in the disease for early diagnosis. A monocytic exudate in the pharynx or sputum and the isolation of one of the causative viruses or serologic evidence of its activity are pathognostic.

DIFFERENTIAL DIAGNOSIS

The most important diseases to consider are pneumonias of bacterial origin, pulmonary tuberculosis and neoplasm, histoplasmosis, coccidioidomycosis, psittacosis, Q fever, typhoid, toxoplasmosis, allergic pneumonia, rheumatic pneumonia and erythema multiforme exudativum. Most of these entities can be recognized by their epidemiologic or clinical behavior, history of exposure and by appropriate laboratory procedures (Figs. 4 and 5). Roentgenography cannot be depended upon for early differentiation. Diagnostic reliance on therapeutic trials with antimicrobics is not recommended except in special circumstances. It is of greatest importance to discover the cause and to select specific therapy for the case at hand.

The commonest diagnostic problem involves differentiation from clinically atypical pneumococcic pneumonia and if pneumococci are found in the sputum. Pneumococci, especially of the higher numbered types, may be present as commensals during viral pneumonia.

PREVENTION

Basic respiratory tract diseases and their pneumonic forms caused by some of the newly isolated adenoviruses may be prevented by specific vaccines. The duration of the immunity evoked probably is short. The matter still is in the experimental stage.

The contagiousness of most of these infections suggests the need for isolation of the victim, but measures usually are enforced too late to be effective. Avoidance of contact if possible is advisable. Aerosols or ultraviolet light applied to the atmosphere in closed quarters may provide temporary protection but generally are impracticable. Chilling, fatigue and previous infection of the respiratory tract, except in certain instances, are not important predisposing factors.

Antimicrobic prophylaxis with currently available agents is illogical for viral infections and is of little or no value in preventing bacterial invasion. It is better to anticipate and treat bacterial infections specifically if they arise.

TREATMENT

Aching may be controlled with codeine sulfate in doses of 15 to 30 mg. Analgesic drugs such as aspirin cause diaphoresis, which already may be present and annoying. Dryness of the nose and throat may be relieved by the inhalation of steam or a spray of warm isotonic solution of sodium chloride. Nasal obstruction may be reduced with a 1 per cent aqueous solution of ephedrine sulfate or with solution of epinephrine hydrochloride sprayed into the nares or by inhaling vapor from a commercially prepared inhalator containing amphetamine or other decongestant at intervals when necessary. Cough may be relieved with menthol lozenges, inhalation of steam with or without aromatics, by the inhalation of oxygen and 5% carbon dioxide or codeine sulfate. Since the nature of the infection usually is not catarrhal, it is never necessary to use expectorants or cough syrups in the hope of favoring expectoration. Severe cough may be lessened temporarily by a laryngeal or intratracheal spray of 0.5 cc. of

0 5% solution of a mono p chlorphenol in oil An abdominal binder and an icecap are comforting For dyspnea and cyanosis a cool moist atmosphere of 40 to 70% of oxygen furnished by means of a tent or otherwise is recommended

Circulatory collapse and pulmonary edema are treated appropriately The best that can be done is to control the infection itself or to support the patient by heat to keep the body temperature near normal Vasopressor agents (arterenol norepinephrine) 4 to 8 cc in 1 000 cc of fluid given intravenously by the drip method may be used with caution The injection of fluids or plasma seldom is of benefit unless there is dehydration Cardiac stimulants, atropine or morphine may be harmful Venesection is contraindicated except for plethora Convalescent serum and roentgen therapy have no value, nor has transfusion of blood unless there is severe anemia

According to controlled studies none of the available antimicrobic agents has any influence on the course of viral pneumonia [5,6] When doubt arises about pneumococcic or other pneumonia, antimicrobic therapy as described on page 151 or on other appropriate pages should be applied accordingly If no improvement ensues after 48 hours the drug should be stopped There is no indication for the use of adrenocorticotropic hormones

Bed rest during the acute stage and in early convalescence is desirable but there is no need for prolonged restrictions or for special therapy because of residual shadows in the lung

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OTHER VIRAL PNEUMONIAS

INFLUENZAL PNEUMONIA

Influenzal pneumonia was the first recognized primary viral infection of the lung Bacteria free pneumonia was observed at necropsy during the pandemic of influenza in 1918 and the viruses were discovered after 1933 The name influenzal pneumonia is applicable only if the viruses are the cause The misnamed influenza bacillus is not implicated and is the cause of a different form of pneumonia

Influenza viruses are classified as types A B C and possibly D Each causes epidemics or sporadic cases of acute upper respiratory tract disease As in other similar viral infections discussed in the previous section the lungs occasionally may be involved For unknown reasons the proportion of mild non pneumonic cases to severe pneumonic ones varies greatly in different reported epidemics In some outbreaks pneumonia presumably purely viral in origin occurred in 70% of patients in others in none Viral pneumonia probably occurs in 5 or 10% of cases of influenza as it did in the widely publicized epidemic of mild influenza A in 1957 unfortunately called Asian influenza It would be recognized more often if roentgenograms were made routinely

No satisfactory explanation has been given to account for the high incidence of fatal pneumonia caused by secondarily invasive pyogenic bacteria in the pandemic of disease believed to have been influenza in 1918–19 and why bacterial pneumonia so seldom accompanied succeeding epidemics

The clinical characteristics of influenzal pneumonia are similar to those of other viral

pneumonias as described on page 130 On certain occasions infection with influenza virus more than others seems to favor secondary bacterial invasion[2,3] When this occurs any of the pyogenic bacteria at hand at the time may become pathogenic If superinfection is caused by the usual culprits namely pneumococci[4] staphylococci[3] hemolytic streptococci or H influenzae the pneumonia assumes the characteristics of the respective bacterial infection Often a mixture of bacteria is operative causing an uncharacteristic form of pneumonia In many instances of bacterial pneumonia tests reveal evidence of preceding or concurrent infection with influenza virus[5]

The mortality rate of influenzal pneumonia as such is low The rate is higher when bacteria are invasive and depends on the bacteria involved the age and condition of the victim and the use of antimicrobic therapy There is no evidence that prophylaxis with antimicrobics during influenza reduces the incidence of bacterial pneumonia Specific influenza vaccines prevent influenza only if homologous strains are involved At present vaccination to prevent influenza is in an experimental stage

The methods of diagnosis and treatment are the same as described for viral pneumonia page 133

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VIRAL PNEUMONIA OF INFANTS

Several forms of pulmonary infection of unknown cause described in infants have been tentatively called viral pneumonias because of their resemblance to known viral pneumonias Goodpasture and his associates studied a form of pneumonia which often follows certain infectious diseases Intranuclear inclusion bodies characteristic of many viral diseases were found in the epithelial cells of the respiratory tract (Fig 6) The infection is not



Fig 6 Viral pneumonia of infants A cytoplasmic inclusion body is in a bronchial epithelial cell (Courtesy of Dr John M Adams) (From Reimann *Pneumonia* Springfield Thomas 1954)

caused by the virus of herpes simplex nor is it related to the so called inclusion disease of infants

Adams reported epidemics of primary viral pneumonia in infants[1] The disease appeared to be viral in origin because of its epidemiology clinical behavior the presence of cytoplasmic inclusion bodies in the epithelial cells of the respiratory passages and a mononuclear cell exudate The mortality rate was reported as 20% but subsequent studies indicate that many unrecognized mild pneumonic and nonpneumonic forms of the same disease occur Furthermore the infection may be related to disease of adults particularly of the mothers who occasionally had mild infection of the respiratory tract with inclusion bodies in the epithelial cells at the time the infants were sick

Pinkerton and his associates described a still different kind of giant cell pneumonia in infants characterized by interstitial invasion

with large multinucleated cells and cytoplasmic inclusion bodies in the epithelial cells No nuclear inclusions were seen Histologically the changes resemble those found in measles and in distemper in dogs They may be specific or may be caused by various agents, or modified by a deficiency of vitamin A Similar cases have been observed in adults[2,3] One of the causes may be the salivary gland virus,[3] but the inclusions are thought by Hamperl to be protozoa, Pneumocystis carinii According to Enders, a virus isolated from two patients caused cytopathogenic changes in tissue culture which were indistinguishable from those caused by the virus of measles[4]

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SYSTEMIC VIRAL DISEASES WITH PNEUMONIA

Among the viruses which cause systemic disease and pneumonia with characteristic involvement of the skin or mucous membrane are *those of measles*[1,2] variola,[3] varicella,[4] and vaccinia The virus of lymphocytic choriomeningitis also may cause systemic disease and pneumonia[5] The diseases themselves have distinctive characteristics which need not be recited here and the specific pneumonia of each is so similar pathologically and clinically that a single description suffices The psittacosis group of diseases are classed separately from those caused by the true filtrable viruses and are discussed in another section

The pneumonic inflammation affects chiefly the interstitial tissue and is predominantly an infiltration of monocytic cells It is indistinguishable from the pneumonias caused by miyagawanellae, rickettsiae, toxoplasmae, fungi, certain bacilli and certain inhaled irritants There are patches or nodules of soft consolidation often hemorrhagic and confluent particularly about inflamed bronchioles The bronchial and alveolar walls are inflamed and infiltrated with mononuclear cells, lymphocytes, plasma cells, polymorphonuclear cells and erythrocytes Adjacent alveoli contain a thin exudate and desquamated epithelium Cytoplasmic inclusions may be found In measles the characteristic Aligna cell is present Bacteria as secondary invaders often are present, especially in the late stage

It is chiefly in the severe forms of systemic viral diseases that pneumonia occurs The signs and symptoms of pulmonary invasion may be dominant or obscured by the characteristics of the respective disease, or so insignificant as to be ignored Pneumonia no doubt occurs more often than is generally believed and could be detected by routine roentgenography There is cough with or without sputum, a sense of oppression in the chest, dyspnea and cyanosis The pneumonia is clinically and roentgenographically uncharacteristic, consolidation is rare but may be simulated by the confluence of inflamed areas

Pneumonia is the chief cause of death in the viral diseases mentioned, or at least pneumonia is present in the majority of fatal cases studied at necropsy Literature on the subject is reviewed elsewhere[7]

Therapy of these pneumonias is the same as for viral pneumonia

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PNEUMONIA IN INFECTIOUS MONONUCLEOSIS

Most observers regard infectious mononucleosis as a viral disease which indeed it appears to be except for final proof In one series of 500 cases pneumonia was detected in about 3% of cases [1] The pneumonia is rarely a dominant clinical feature and is indistinguishable from other viral pneumonias except for the peculiarities of the disease itself In several patients the disease was mild in spite of extensive pulmonary involvement as demonstrated roentgenographically The pneumonia may be caused by the same agent or by superimposed bacterial infection A rise in the heterophile agglutinin titer characteristic of infectious mononucleosis occurred in several patients with "viral pneumonia of unknown cause yet no abnormal leukocytes or mononucleosis appeared In one case pneumonia characterized by focal cellular infiltration was found at necropsy [2]

PNEUMONIA OF ERYTHEMA MULTIFORME EXUDATIVUM

Pneumonia is present in most cases of erythema multiforme exudativum It is characterized by a mononuclear cell exudate like other viral pneumonias and is believed to be an integral part of the disease which presumably is caused by a virus The lesions resemble those of human foot and mouth disease and also may be mistaken for Vincent s infection because of the presence of fusospirochetal micro organisms in the mouth It is probable that certain cases diagnosed as viral pneumonia with severe mucocutaneous eruptions are actually those of the disease in question [3] It is also called dermatostomatitis mucocutaneous fever mucosal respiratory syndrome and Stevens Johnson disease

PNEUMONIA WITH POSITIVE WASSERMANN TEST

(Fanconi Hegglin Syndrome)

Swiss observers report on a curious form of pneumonia charactĕrized by a positive reaction of the blood when the Wassermann test is made [4] The disease apparently is endemic and epidemic at times affecting members of closely associated groups There often is evidence of nasopharyngitis sometimes without pneumonia In pneumonic cases fever seldom is high and signs of pneumonia are present The leukocytes are normal in number but the sedimentation rate is rapid Roentgenography reveals diffuse shadows sometimes in all lobes and the tracheobronchial lymph nodes are enlarged Infiltration may persist for months The reaction to the Wassermann test stays positive as long as pulmonary lesion lasts The reaction is thought to be dependent upon an increased amount of globulin Cold agglutination of erythrocytes does not occur The disease is self limiting

REFERENCES

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pneumococcic infections were brought about by antimicrobic therapy after 1938 when sulfapyridine, and later, penicillin were introduced. While the death rate diminished from 30% to less than 10% (Fig. 1), the incidence of pneumococcic pneumonia has not declined proportionately.[1] It is estimated that, at present, about one million cases and 50,000 deaths occur annually in the United States.

Etiology

There are 75 serologic types and subtypes of the pneumococcus, of which types I, II, III, V, VII, VIII and XIV are the most important and account for about 80% of typical lobar pneumonias in adults. Among children, types I, VI, XIV and XIX are chiefly responsible. Other numbered types of pneumococci seldom cause primary pneumonia, and in contrast with the ones mentioned are found often in the oropharynx of normal people. They are the chief causes of endogenous or secondary pneumonias and usually give rise to a disease pattern regarded as clinically atypical. Under some circumstances the low numbered types also cause atypical pneumonia. Since modern antimicrobic therapy affects all pneumococci, laboratory determination of the type is unnecessary. Typing is of value however, in diagnosis, for prognosis and for epidemiologic reasons.

Penicillin in proper concentration is bactericidal and rapidly eliminates pneumococci from the sputum and blood. Other antibacterial agents are bacteriostatic. Pneumococci have not become resistant to any of the drugs.

Pneumococcic lobar pneumonia develops when a number of factors or conditions coincide. The necessary ones are (1) a susceptible host, (2) virulent pneumococci, and (3) means of access of pneumococci to the host. Because many persons who carry pneumococci as commensals do not get pneumonia, there appears to be a natural or acquired immunity which prevents invasion and infection. Immunity or resistance may be inherent or may accrue from previous mild pneumonic or non pneumonic infections with pneumococci. Repeated exposure to pneumococci or their continued presence may lead to a variable degree of specific hypersensitivity of the host to the cocci or to the products of their growth, the nature of which is poorly understood. Before invasion can occur, conditions in a person obviously change to enable the pneumococci to multiply, to become invasive and cause the train of circumstances culminating in lobar pneumonia. Factor 3 or the access of pneumococci to the host is discussed under the heading Epidemiology.

So far as is known, invasion of the lungs by pneumococci does not take place directly. Some injury apparently must prepare the field to permit invasion. In the case of lobar pneumonia, minor infections of the respiratory tract are the most obvious causes of "reduction of resistance." Changes in the state of the mucosa of the respiratory tract brought about by sudden chilling, by volatile irritants, by trauma and by other means also are predisposing factors. Theoretically, changes in the membrane may be brought about also by complex sympathetic nervous or vasomotor reflexes caused by various stimuli. Lobar pneumonia may be initiated by concussion of the chest wall and by aspiration of liquids.

Epidemiology

Lobar pneumonia occurs in all age groups, most frequently in early and middle adult life. In general hospitals, before the modern therapeutic era, most of the patients admitted were in the age group of 30 to 50, since then patients in the 40 to 60 year group predominate. The change may be attributed to several factors: the successful treatment of younger patients at home, the unchanged incidence of the disease and unsuccessful treatment in older persons especially in those with complicating degenerative or other chronic diseases, chronic alcoholism, and the advancing age of the general population. Ma more often are affected. Pneumonia occu more often in cold months probably becaus predisposing minor infections of the respiratory tract are common then. Occupation has but little effect. Lobar pneumonia occurs in the Frigid, Temperate and Torrid Zones.

Although the incidence of pneumococcic lobar pneumonia is remarkably constant, fluctuations in numbers of cases are noted from year to year, generally or locally, depending

on the prevalence of predisposing minor infections of the respiratory tract and the prevalence of different types of pneumococci. The disease usually appears sporadically, but occasionally several members of family or other intimate groups may be infected at once or in rapid succession in small epidemics. Types I, II and V pneumococci usually are responsible. During epidemics some victims may have lobar pneumonia, others may have bronchitis or sinusitis. Pneumococci of same type may be present in the nose and throat of other exposed persons who remain well. They become temporary carriers of types of pneumococci which rarely are found in normal persons otherwise. In such instances there is clear evidence of contagiousness since the same type of pneumococcus is involved. In general, however, pneumococcic pneumonia seldom is transmitted directly and patients with it usually can be treated at home or in medical wards of a hospital without serious danger of infecting others.

Carriers

To account for their perpetuation pneumococci obviously must reside as commensals perennially in permanent or temporary carriers. The types of pneumococci commonly implicated in pneumonia (I, II, III, V, VII, VIII and XIV) rarely are found in normal persons excepting those in close contact with disease caused by pneumococci of the same type. It is estimated that about 60% of normal people carry pneumococci of the less invasive higher numbered types in their oropharynx. The number of carriers often increases temporarily during epidemics of colds. Patients convalescent from pneumonia harbor pneumococci for variable periods afterward.

Mode of Spread

To cause pneumonia, pneumococci must come in contact with the victim. Pneumococci may have been present in the air passages and cause endogenous infection, but in lobar pneumonia exogenous infection is the rule. The source of pneumococci obviously is the patient or the healthy carrier who expels pneumococci attached to fine droplets of secretion by talking, sneezing, coughing or otherwise. As the droplets dry, microscopic particles bearing pneumococci float about in the air much like tobacco smoke and these are inhaled by persons in the vicinity. The inhaled pneumococci may be entangled in the cilia and secretion of the air passages and promptly die or are expelled, or may take up residence if conditions permit. Pneumococci also may be spread by eating utensils, handkerchiefs or anything contaminated with pneumococcus laden material. Pneumococci have been cultivated from expectorated sputum collected from the street. They remain viable for days in dust or when suspended in the air but eventually succumb to prolonged drying, exposure to sunshine or to chemicals.

Pathogenesis

Pneumococci alone or attached to minute airborne particles may reach the lung and enter the alveoli. From roentgenographic evidence the earliest lesion occurs anywhere in the lung. It is assumed that a small lesion develops around the place where pneumococci begin to grow and infection spreads throughout a lobe by way of the lymphatics. In many instances pneumococci invade the blood stream. No satisfactory explanation accounts for the massive involvement often confined to one lobe or why the clinical manifestations are suddenly so severe. An allergic basis and an explosive anaphylactic-like reaction of tissue sensitized by previous exposure to the same antigen has been suggested as a reason. The reaction and clinical symptoms are less violent in persons who are debilitated from other causes and the resulting pneumonia as a rule is atypical.

Pathology

Traditionally the pathologic changes in the lung of lobar pneumonia pass through four phases: engorgement, red hepatization, grey hepatization and resolution. The sequence rarely is so clear-cut. The inflammatory process may be at different stages of development in different lobes or in the same lobe. A whole lobe, several lobes or only part of a lobe may be involved.

The initial lesion usually appears near the periphery and spreads. In induced pneumonia

in animals, it consists of a small area of inflamed alveoli full of serous fluid, pneumococci, leukocytes, erythrocytes and desquamated cells of mesodermal or endodermal origin. The capillaries are distended. Inflammation spreads from alveolus to alveolus directly or by way of pores, lymphatics and blood vessels or is carried through the air passages by infected exudate. In this state of engorgement, the involved lung is heavy, congested and dark bluish red. A thin foamy, cloudy, pink exudate is present.

The stages of hepatization are so named because of the resemblance of the pneumonic area to liver. In the red stage the lesion is firm, friable, dark-red and airless. The cut surface is drier than before and a turbid reddish exudate can be scraped off. Microscopically there is more fibrin and the alveoli are packed with polymorphonuclear leukocytes, red cells and pneumococci enmeshed in fibrin. The area is hyperemic. After a day or two the redness turns to gray. Hyperemia is less and the area is drier. Microscopically the involved alveoli almost are obliterated by polymorphonuclear leukocytes and masses of fibrin. Large mononuclear cells now appear. The tissue is anemic.

In the stage of resolution, the consolidated tissue softens, liquefies and slowly disappears by resorption or otherwise. Many large phagocytic mononuclear cells appear in the alveolar walls, air spaces and regional lymph nodes. Soon the alveolar epithelium regenerates and after 8 to 14 days is normal again. In rare instances resolution is delayed or ends in permanent fibrosis. Abscess formation is rare except in type III pneumococcic pneumonia of long duration.

The right lung most often is affected. In infancy and childhood often only part of a lobe is involved and consolidation is not so firm as in adults.

Changes in the Bronchi, Pleura and Elsewhere

The bronchi and bronchioles in the pneumonic area usually contain purulent exudate, but seldom are inflamed. The pleura over the pneumonic area may be inflamed and later covered with fibrin of variable thickness. The pleural cavity may contain serous fluid with polymorphonuclear leukocytes, lymphocytes, desquamated endothelial cells and debris. When the fluid is infected with pneumococci (empyema) it becomes purulent and creamy. The bronchial and tracheobronchial lymph nodes may be inflamed and swollen. Histologic evidence of myocardial injury is found occasionally. Sterile or infected pericarditis may be present, often in connection with pleuritis. Ulcerative endocarditis, purulent arthritis and meningitis may occur. There may be cloudy swelling of the liver and spleen and mild glomerulitis.

Symptomatology

Pneumococcic pneumonia in its lobar form is a remarkably uniform disease. At the onset in most instances, there is a history of a mild infection of the respiratory tract, but a new series of events heralding pulmonary invasion suddenly occur. They constitute the five cardinal features of lobar pneumonia, namely *a shaking chill, pain in the chest, cough, sputum and fever*. They may all appear at once, or in sequence, or one, several or all may be absent. In some patients, particularly old ones or ones debilitated by chronic diseases, the onset may be gradual.

In the classic or model case, there is a single *shaking chill* which lasts from several minutes to an hour (Fig. 7). Less often chills recur or consist only of shivering or a chilly sensation. The temperature rises rapidly to between 38°C and 40.5°C (103°F and 105°F), often reaching its height during the first 12 hours. The patient is flushed, the skin is hot and dry. Sweating seldom occurs. The pulse rate and respiration rate increase, and there are headache, malaise, anorexia, nausea and perhaps vomiting and diarrhea. *Pleuritic pain* may be the first symptom, and occurs at some time in most patients. It usually is in the lower part of the chest and may be severe and made worse by breathing or coughing. It causes respiration to be restricted and each breath may be accompanied by a grunt of pain and flaring of the nostrils. Pain may be referred to the abdomen, especially in children, and suggest appendicitis. Dyspnea, anoxia and cyanosis often, but not always, are in propor-

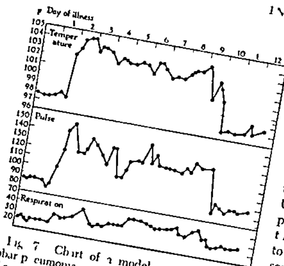


Fig. 7. Chart of a model case of untreated lobar pneumonia caused by pneumococcus type I observed in 1936. A man aged 23 had a sudden chill followed by vomiting and cough. Leukocytes numbered 24 000 and 34 000. Dullness, harsh breath sounds and rales were audible on the first day in the right middle lobe where increased density was revealed in a roentgenogram. Signs of consolidation were present on the third day. Spontaneous crisis occurred on the tenth day. (From Bermann: *Pneumonia*, Springfield, Thomas, 1954.)

tion to the extent of pulmonary involvement. Herpes may appear on the lips or elsewhere.

The *cough* at first may be dry, hacking, paroxysmal and unproductive of sputum. It disturbs sleep, increases pleuritic pain and headache and soon causes soreness of the abdominal muscles. In infants or in debilitated patients cough may be weak or absent. *Sputum* may be raised shortly after the onset. It may be purulent, yellowish white, pink or streaked with blood. Later it becomes brown, tenacious, difficult to raise and adherent to the container. The amount usually is small. There may be no sputum.

Physical Signs

In the earliest period the patient may or may not appear to be seriously sick and lies on the affected side to minimize pleuritic pain. There may be dyspnea, tachypnea and apprehension. The face is flushed, the nostrils dilate with each grunting breath, the lips may be bluish and show herpetic vesicles. The oropharynx is reddened and dry.

The earliest abnormal signs in the chest are limitation of respiratory motion of one side if pleuritic pain is severe and compensatory expansion of the sound side. Unless congestion of a lobe is advanced, tactile fremitus is slightly impaired if at all. Percussion may reveal impairment of resonance. The breath sounds in the inflamed area may be suppressed and fine rales are audible. Often within a few hours or a day as hepatization progresses the characteristic signs of consolidation evolve. Unless pleuritic pain is present both sides expand equally. There are an increase of tactile fremitus over the pneumonic area, dullness to percussion, bronchial or tubular breath sounds and bronchophony, egophony and pectoriloquy. Rales seldom are prominent. Pleural friction may be audible. The blood pressure may rise, fall or remain unchanged. Tachycardia is the rule.

Roentgenographically changes in the pneumonic area appear within a few hours after the onset as a diffuse veil-like haziness which becomes denser and spreads in a matter of hours. The shadow often is triangular in shape with its base at the periphery. Consolidated areas usually are sharply delineated as homogeneous dense shadows confined to a lobe or lobes bounded by the pleural envelop. Roentgenographic evidence of pneumonia often precedes the development of abnormal physical signs. Films made in the lateral as well as antero-posterior position should be viewed to locate the lesion.

Laboratory Data

The number of leukocytes and the percentage of polymorphonuclear leukocytes begin to increase promptly after the onset and often reach 20 000 or more the first day. The blood platelets decrease in number. The sedimentation rate of erythrocytes increases within a few hours and reflects an increase in the amount of fibrinogen and globulin in the blood. Both features are more pronounced in pneumococcic pneumonia than in any other common infectious disease. The sputum usually is tenacious, rusty and microscopically there are many fresh or degenerated leukocytes, mostly polymorphonuclear, red cells, pneumococci and a variety of other bacteria. In some cases pneumococci may predominate

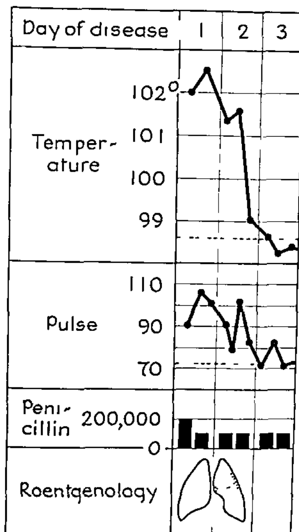


Fig 8 Lobar pneumonia treated on the first day The patient, aged 25, had a cold for 10 days before a shaking chill lasting 90 minutes occurred at 6 a m A few hours later severe headache cough, fever, and pain in the left mammary region were noted He vomited once Admitted to hospital soon afterward In the left mammary region there were diminished breath sounds and rales where a roentgenogram revealed a shadow There was a small amount of sputum blood streaked from nosebleed Leukocytes numbered 19 000 Because of the clinical diagnosis of lobar pneumonia, penicillin in amount of 200 000 units (120 mgm) was injected intramuscularly on the first day of disease, and 100 000 units (60 mgm) every 12 hours for three days Pneumococci recovered from a mouse's peritoneal cavity on the second day were of type XIII The temperature fell to normal on the second day and no further abnormal signs developed in the chest (From Reimann *Pneumonia* Springfield, Thomas, 1954)

or appear to be present alone Pneumococci are present in the blood in from 35 to 50% of cases, as shown by blood culture

The foregoing clinical description of the early phase of lobar pneumonia is presented in considerable detail because so much depends on the early recognition of the disease and the prompt selection and use of an appropriate therapeutic agent Discussion of the subsequent course is divided into a description of the natural course of the disease when untreated and the course as modified by therapy

Natural Course of Lobar Pneumonia

The natural course of a model case of lobar pneumonia is illustrated graphically in Figure 7 Shortly after the onset, the severity of the early symptoms and signs increases The temperature remains at a high level or occasionally is remittent or irregular, with or without chills and sweating Fever may increase as other lobes are affected, or if purulent localization involves the pleurae, joints, meninges, endocardium or other area The severity of the disease usually, but not always, is in proportion to the extent of the pulmonary lesion Dyspnea and cyanosis may increase, tachycardia and tachypnea persist Pleural pain may appear or if present may disappear Delirium, vomiting, abdominal distention, hiccough may be distressing and serious

Death may be caused by "toxemia," exhaustion, circulatory collapse or by complications In those who recover, the course in about 70% of cases lasts from 5 to 9 days Disease of longer duration may be caused by type III pneumococci, and, of course, when purulent complications occur Abortive attacks may last less than a day Spontaneous crisis marks a change from severe sickness to recovery within a period of several hours The temperature and pulse rate fall rapidly to normal (Fig 7) and there is profuse sweating In other instances lysis occurs with a gradual disappearance of abnormal signs and symptoms

The Course of Lobar Pneumonia When Treated

Antimicrobial agents alter the course of

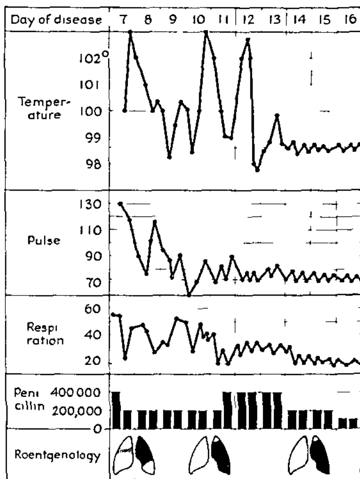


Fig 9 Type I pneumococcic pneumonia treated late in the disease. The patient aged 27 had a "head cold" for two weeks which "spread to the chest." There was cough and brownish sputum, chilly sensations and sweating. Severe pain on breathing in the left side obliged the patient to come to the hospital on the seventh day of severe disease. He was toxic, very sick, dyspneic and tachypneic. There were signs of consolidation of the left upper lobe. A dense shadow in that area and a fainter shadow in the right lung were revealed roentgenographically. The leukocytes numbered 23 000 and the sedimentation rate was increased. Type I pneumococci were present in the sputum.

Because of the severity of the disease and delay in treatment 400 000 units (240 mgm) of penicillin were injected intravenously as a first dose and 200 000 units (120 mgm) twice daily thereafter. As indicated by the fever curve there was a therapeutic response on the ninth day but high fever recurred on successive days without proportionate tachycardia. Some purulent localization (empyema?) was suspected but not proved. Roentgenographically the lesion spread to the rest of the left lung during therapy. The dose of penicillin was increased on the eleventh day but recovery did not occur until the thirteenth day. Apparently delay in beginning treatment and a spread of pneumonia were responsible for the prolongation of disease even under apparent adequate dosage of penicillin. (From Reimann *Pneumonia* Springfield Thomas 1954)

pneumococcic pneumonia. When diagnosis is made promptly and therapy given in adequate dosage the course of the disease usually is shortened. Pneumococci disappear rapidly from the sputum and blood. Recovery in about one half of the patients occurs within 24 hours after treatment is started and within 48 hours in nearly 80% (Fig 8). Occasionally several days elapse before the temperature becomes normal (Fig 9). The pulmonary inflammation in patients who recover early may not progress to the stage of consolidation or it may continue to evolve through the phase of consolidation even though the patient is symptom free. Usually resolution begins promptly. In a small percentage of cases the disease progresses to a fatal end despite apparently adequate therapy. This outcome most often occurs in debilitated infants, in the aged, in chronic alcoholics, in debilitated patients with pneumonia caused by type III pneumococci, when there is bacteremia or multilobar involvement, when therapy is delayed too long or is given in subminimal doses and if purulent complications or other disease are present.

The reproduction of several hospital charts

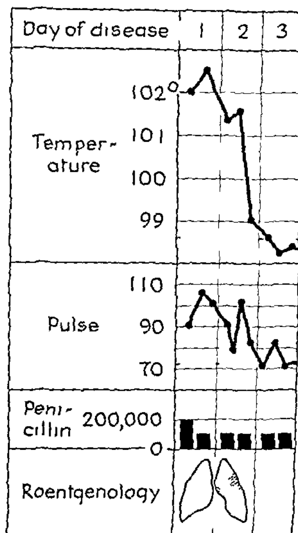


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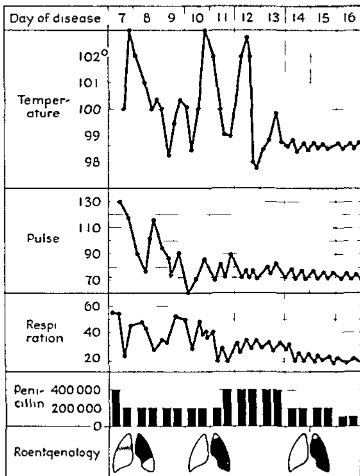


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The reproduction of several hospital charts

on adjacent pages illustrate some of the favorable and some less favorable responses to therapy which cause concern and require therapeutic judgment In several patients treated early, recovery was postponed beyond the expected termination of disease When fever persisted more than 48 hours while apparently adequate dosage was used, the development of extrapulmonary purulent

The case illustrated in Figure 10 was atypical in nature and caused by type XIII pneumococci Probably because of the age of the patient with *chronic alcoholism and bronchiectasis*, recovery did not occur until the eleventh day Figure 11 illustrates the success of therapy with penicillin in an infirm, aged *patient in whom death otherwise would have* been regarded as inevitable The patient was

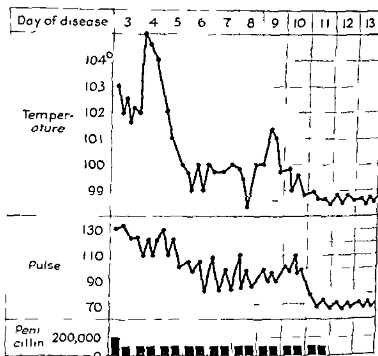


Fig 10 Pneumococcic pneumonia, atypical in nature The patient aged 49, was an alcoholic and had bronchiectasis He had a cold in *December and on* January 1, had chilly sensations most of the day On January 2, fever, profuse sweating, dyspnea and sharp pain on breathing in *his left axilla were noted* He entered the hospital on January 3

He was seriously sick, flushed and trembling (delirium tremens), the skin was hot and moist There were dullness fine rales, increased breath sounds and friction over the left lower lobe The leukocytes numbered 16,000 Pneumococci were not recovered directly from the sputum, but inoculation of mouse later revealed type XIII pneumococci

Penicillin was administered intramuscularly Although the *temperature declined and symp*toms improved on the fifth day, fever and tachycardia persisted until the tenth day Friction was audible until the twelfth day Recovery took place gradually

In this case pneumonia assumed the atypical form in a patient aged 49, whose resistance was poor Therapeutic response to penicillin was low (From Reimann *Pneumonia* Springfield, Thomas, 1954)

localizations was suspected These may occur and may be cured by continuing treatment or by increasing the dose

Figure 9 illustrates an instance in which belated treatment may have interfered with the expected response to penicillin During therapy with large amounts of penicillin, pneumonia spread to other parts of the lung Empyema was suspected Recovery was delayed until the thirteenth day

not treated for pneumonia until the sixth day and 2,700 colonies of pneumococci per cc grew in a blood-agar culture plate

The course in certain patients, particularly in infants and in the aged, may end fatally despite modern therapy, indicating that the control of infection alone is not enough and that the support of *the forces of natural* defense must be aided by other methods not yet available

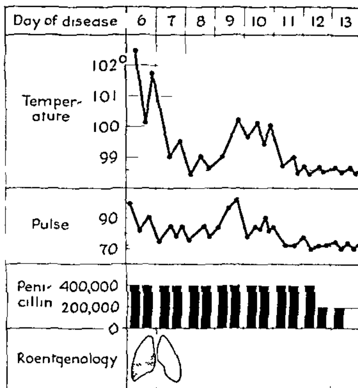


Fig 11. A typical type VI pneumococcic pneumonia with bacteremia in a senile patient. A man aged 73 had a fractured femur which kept him sedentary for four years. About February 4 he began to cough and raise white, occasionally brown, sputum. Generalized aching and dull thoracic pain were noted. He was sent to the hospital six days later chiefly because of pain in the hip. Examination revealed fever, tachycardia and dyspnea. He responded sluggishly to questions but was in no distress. A few rales were audible in the right base where a density was revealed roentgenographically. The leukocytes numbered 8,000 and the sedimentation rate was rapid. No sputum was raised. Asthenic or senile pneumonia was suspected and large doses of penicillin were administered intramuscularly. A blood culture revealed 2,700 colonies per cc of type VI pneumococci. Therapy was continued and blood obtained on the ninth day was sterile. Considering the patient's age, his infirmity and the intense bacteremia, death almost certainly would have occurred if penicillin had not been used. (From Reimann, *Pneumonia*, Springfield, Thomas, 1954.)

PNEUMONIAS AS SEPARATE ENTITIES ACCORDING TO PNEUMOCOCCUS TYPE

Pneumococci of type I cause 25% of all lobar pneumonias and usually give rise to the most "typical" cases. When the pneumonia is "atypical" the prognosis is worse. Complications occur in 22% of untreated patients, chiefly empyema. The mortality rate was 12% and with bacteremia 80%.

Type II pneumococcic pneumonia behaves like that of type I except for a higher incidence of bacteremia (40%), a longer duration and a mortality rate of 26% or 89% when the blood culture is positive in untreated patients. Endocarditis occurs in about 2% of untreated patients.

The type III pneumococcus causes pneumonia which differs in certain respects from the disease caused by the type I or type II pneumococcus.[4] Some physicians look upon type III pneumonia as a separate disease. This pneumococcus for some unknown reason is found more often in the normal nasopharynx in health than any other important type of pneumococcus excepting type VI. It is one of the most common causes of chronic infection of the respiratory tract, of the middle ear and of the mastoid cells. Because of its prevalence in the nose and throat it is one of the bacteria which may become invasive as soon as a reduction of resistance of the host permits. It is therefore a frequent cause of pneumonia in debilitated or senile patients and in those with other acute or chronic disease of the respiratory tract. Postoperative pneumonia often is caused by type III pneumococci.

As a cause of pneumonia, the type III pneumococcus ranks third in importance In some large series of cases, it ranks second, with type II third The highest incidence of infection is in the fifth decade and 70% of patients are over the age of 40

The onset is sudden (70%) in most cases of the lobar form and gradual (60%) in the atypical form Chill, pain and rusty sputum are present in three quarters of the cases The onset of atypical type III pneumonia usually is gradual with fever, cough or dyspnea, and the *symptoms often merge with those of the* primary condition The blood culture is positive in about 35% of cases The disease if treated or untreated lasts longer than other pneumonias In about one third of patients who recover from the lobar form the disease ends by crisis Crisis seldom occurs in patients over the age of 50 Type III pneumonia is an uncommon and mild disease in childhood Complications occur in about 20% of cases Empyema and pericarditis are the *commonest* Lung abscess, though frequent, usually is discovered only at necropsy

The death rate is higher in type III pneumonia than in any other type but this is accounted for by the fact that it occurs so often as a disease secondary to other serious conditions[4] The mortality rate is between 40 and 60%, but if only young persons without other illness and under the age of 40 are considered, the mortality is less than 15%

Untreated patients with type III pneumonia and bacteremia almost without exception die The death rate without bacteremia is about 34%

OTHERS

Clinical differences of pneumonia caused by other important types of pneumococci (V, VII, VIII, and XIV) have no special characteristics and need no special discussion Type V pneumococci are related serologically to type II, and type VIII pneumococci to type III Type XIV is of especial importance in infancy and childhood wherein it causes 20 per cent of cases

PNEUMOCOCCIC ATYPICAL PNEUMONIA

In certain patients, pneumococci do not cause the signs and symptoms of classic lobar pneumonia The pneumonia has no outstanding clinical characteristics and resembles that which is caused by a variety of other germs Patients in whom pneumonia takes the atypical form usually are senile or debilitated by some other chronic malady and do not react to infection in so vigorous a manner as otherwise normal persons do It develops also in patients in whom some other severe infection, such as measles or influenza, injures the lungs and the defensive mechanism profoundly enough to permit secondary invasion by pneumococci The fact that the higher numbered types of pneumococci, as commonly found in the normal oropharynx, are the usual causes further indicates the endogenous nature of the infection Low numbered pneumococci less often cause the atypical form of pneumonia

Symptoms

The onset usually is gradual and merges with the predisposing condition (Figs 9 and 10) Chilliness or a series of chills rather than a single shaking chill occur There may be substernal pain or oppression, there is cough with scanty sputum which is not so tenacious as in the lobar form The fever rises slowly and is irregular, with occasional elevations as the process spreads in the lungs Both lungs often are affected, chiefly in the lower lobes The severity of an attack varies greatly depending somewhat on the gravity of the underlying or predisposing disorder The course may end after a few days or may last many weeks either continuously or with remissions and exacerbation In favorable cases, recovery occurs by lysis Complications and bacteremia occur less often than in lobar pneumonia Necrosis and abscess of the lung occur in cases of long duration

The physical signs are variable and change slowly or rapidly from place to place as the process spreads Areas of atelectasis are common *The signs over the affected areas are* those of congestion with dullness, suppression of breath and voice sounds and numerous

rales When pneumonic areas merge modified signs of consolidation may be heard Roentgenographically there are patchy areas of infiltration usually bilateral

Prognosis

The mortality rate due to other previous or concurrent disease is usually double that of lobar pneumonia even in comparative groups of patients treated with antimicrobics Antibacterial therapy may control infection successfully but efforts must be intensified to correct the primary underlying disease or to increase the resistance of a debilitated host

Treatment

The specific treatment is the same as for pneumococcic lobar pneumonia An underlying condition if present must be corrected

MIXED OR MULTIPLE INFECTIONS IN PNEUMOCOCCIC PNEUMONIA

Two or more types of pneumococci occasionally are found in the sputum and in the lung of the same patient. Types of pneumococci ordinarily found in health may of course still be present in the sputum during pneumonia caused by another type Other bacteria such as streptococci staphylococci Klebsiella pneumoniae and tubercle bacilli also may be cultivated from the sputum blood or lung of patients with pneumococcic pneumonia The problem which then confronts one is to determine which of the bacteria present is the cause of the pneumonia This uncertainty occurs in about 10% of cases of pneumonia when careful bacteriologic studies are made

The likelihood of obtaining several types of pneumococci or several kinds of bacteria is greatest when the sputum is cultivated on artificial media The injection of sputum into mice serves to eliminate most of the extraneous organisms except pneumococci but even then several types of pneumococci may be encountered Several types of pneumococci also may be found by applying the Neufeld capsule-swelling test to sputum The problem is more perplexing but fortunately rare when more than one variety or type of bacteria is cultivated from the blood stream from material obtained by lung suction or from areas of focal localization in other portions of the body

The problem to decide is (a) whether only one type of pneumococcus is causing the disease and the others are incidental (b) whether more than one variety of organism is causing the disease as concurrent infection or (c) if there is super infection or consecutive infection Factors (b) or (c) in some cases may account for some of the failures noted in patients otherwise properly treated with antimicrobics They may account for prolongation of the illness or for relapses Recurrences of pneumonia may be caused by a different type of pneumococcus or other bacterium from that which caused the preceding attack During therapy with antimicrobics drug resistant bacteria or fungi may become invasive

Hemolytic streptococci and staphylococci may act as secondary invaders in pneumococcic lobar pneumonia to cause septicemia lung abscess or other lesions Conversely in primary hemolytic streptococcic pneumonia in staphylococcic pneumonia or in others the usual types of pneumococci ordinarily found in the nasopharynx may be present in the sputum Under these circumstances the diagnosis is made from the history of the case the clinical course the roentgenographic studies and the nature of the pathologic changes in the lung according to each specific entity The subsequent demonstration of specific agglutinin in the blood against the causative bacteria also is of value In a large proportion of patients with atypical pneumonia several varieties of bacteria always are present in the sputum and lung lesion and it is impossible to determine if any one or if all of the varieties of bacteria found are operative

Recurrence

About 15% of persons who have lobar pneumonia give a history of one or more previous attacks The same type or a different type of pneumococcus may be the cause Different lobes may be involved at different times One attack does not necessarily predispose to another it is more likely that some persons are more susceptible to infection than others

As a cause of pneumonia the type III pneumococcus ranks third in importance In some large series of cases it ranks second with type II third The highest incidence of infection is in the fifth decade and 70% of patients are over the age of 40

The onset is sudden (70%) in most cases of the lobar form and gradual (60%) in the atypical form Chill pain and rusty sputum are present in three-quarters of the cases The onset of atypical type III pneumonia usually is gradual with fever cough or dyspnea and the symptoms often merge with those of the primary condition The blood culture is positive in about 35% of cases The disease if treated or untreated lasts longer than other pneumonias In about one third of patients who recover from the lobar form the disease ends by crisis Crisis seldom occurs in patients over the age of 50 Type III pneumonia is an uncommon and mild disease in childhood Complications occur in about 20% of cases Empyema and pericarditis are the commonest Lung abscess though frequent usually is discovered only at necropsy

The death rate is higher in type III pneumonia than in any other type but this is accounted for by the fact that it occurs so often as a disease secondary to other serious conditions[4] The mortality rate is between 40 and 60% but if only young persons without other illness and under the age of 40 are considered the mortality is less than 15%

Untreated patients with type III pneumonia and bacteremia almost without exception die The death rate without bacteremia is about 34%

OTHERS

Clinical differences of pneumonia caused by other important types of pneumococci (V VII VIII and XIV) have no special characteristics and need no special discussion Type V pneumococci are related serologically to type II and type VIII pneumococci to type III Type XIV is of especial importance in infancy and childhood wherein it causes 20 per cent of cases

PNEUMOCOCCIC ATYPICAL PNEUMONIA

In certain patients pneumococci do not cause the signs and symptoms of classic lobar pneumonia The pneumonia has no outstanding clinical characteristics and resembles that which is caused by a variety of other germs Patients in whom pneumonia takes the atypical form usually are senile or debilitated by some other chronic malady and do not react to infection in so vigorous a manner as otherwise normal persons do It develops also in patients in whom some other severe infection such as measles or influenza injures the lungs and the defensive mechanism profoundly enough to permit secondary invasion by pneumococci The fact that the higher numbered types of pneumococci as commonly found in the normal oropharynx are the usual causes further indicates the endogenous nature of the infection Low numbered pneumococci less often cause the atypical form of pneumonia

Symptoms

The onset usually is gradual and merges with the predisposing condition (Figs 9 and 10) Chilliness or a series of chills rather than a single shaking chill occur There may be substernal pain or oppression there is cough with scanty sputum which is not so tenacious as in the lobar form The fever rises slowly and is irregular with occasional elevations as the process spreads in the lungs Both lungs often are affected chiefly in the lower lobes The severity of an attack varies greatly depending somewhat on the gravity of the underlying or predisposing disorder The course may end after a few days or may last many weeks either continuously or with remissions and exacerbation In favorable cases recovery occurs by lysis Complications and bacteremia occur less often than in lobar pneumonia Necrosis and abscess of the lung occur in cases of long duration

The physical signs are variable and change slowly or rapidly from place to place as the process spreads Areas of atelectasis are common The signs over the affected areas are those of congestion with dullness suppression of breath and voice sounds and numerous

rales When pneumonic areas merge modified signs of consolidation may be heard Roentgenographically there are patchy areas of infiltration usually bilateral

Prognosis

The mortality rate due to other previous or concurrent disease is usually double that of lobar pneumonia even in comparative groups of patients treated with antimicrobics Antibacterial therapy may control infection successfully but efforts must be intensified to correct the primary underlying disease or to increase the resistance of a debilitated host

Treatment

The specific treatment is the same as for pneumococcic lobar pneumonia An underlying condition if present must be corrected

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Delayed Resolution

The consolidated tissue of the lung ordinarily resolves and returns to its normal state within a week or two after recovery. Occasionally a longer time is needed but it is of no clinical significance. Permanent fibrosis rarely occurs. The condition called *unresolved pneumonia* implies the continuation of disease or chronic pneumonia. It often is caused by some underlying disturbance like bronchiectasis, neoplasm, a foreign body, or aneurysm which interfere with bronchial drainage, or by pleural effusion, empyema, abscess or atelectasis.

Diagnosis

Pneumococcic lobar pneumonia is one of the easiest of diseases to diagnose. The history of a cold and the sudden onset of the symptoms and signs listed under symptomatology leaves little doubt. Diagnosis is confirmed by roentgenography and by isolating the causative pneumococcus from the sputum, and blood. Typing of the pneumococcus, although generally abandoned, is of diagnostic aid. The presence of the low numbered types—I, II, III, V, VII and XIV—which seldom are found in normal persons adds great weight to the diagnosis. If sputum cannot be obtained, oropharyngeal secretion obtained by a swab may be tested. The type of pneumococcus, if present, can be determined directly by the Neufeld capsule-swelling test. If difficulty is encountered, sputum should be inoculated intraperitoneally into a white mouse and samples aspirated from the peritoneal cavity at intervals for typing. The presence of other numbered types, unless predominant or in overwhelming numbers is not diagnostic but only suggestive. Pneumococci in the blood of whatever type are most significant. The blood culture is positive in from 15 to 50% of cases. Exudates from the pleural cavity, pericardium, meninges or elsewhere always should be cultured and the bacterium identified. It is of greatest importance to determine promptly whether pneumococci are the cause of the pneumonia in order to select and begin proper therapy. Previous administration of antimicrobics eliminates pneumococci from the sputum and precludes their isolation for diagnosis.

The leukocytes, with polymorphonuclear cells predominant, almost always are increased in number from 12,000 to 30,000. They may be normal or subnormal in number especially in debilitated persons or severe illness. The sedimentation rate begins to increase within a few hours after the onset and reaches rates higher than in any other common infectious disease. The rate slowly returns toward normal after recovery and may not become normal for several weeks.

Differential Diagnosis

Certain diseases in their early period or at some period may be confused with lobar pneumonia. Chief among them are pulmonary infarction or abscess, acute bronchitis, acute pericarditis, pleural effusion, atelectasis, myocardial infarction, Klebsiella or tuberculous lobar pneumonia and pneumonia caused by other bacteria see (Table IV). The absence of pneumococci from the sputum or blood, the presence of other significant bacteria, a history of previous disease in some instances, appropriate studies and tests, and the subsequent course usually serve to differentiate them.

Prognosis

The death rate of untreated pneumococcic lobar pneumonia is about 30%. The prognosis is best in children over 2 years of age and in early adult life. The presence of complications or other debilitating chronic disease is unfavorable. Bacteremia greatly increases the mortality, with differences of as much as 90% as compared with 10%. Pneumonia caused by types III and II pneumococci has the highest death rate, 50 and 44%, respectively.

Antimicrobial drugs when given promptly in adequate amounts reduce the death rate to between 5 and 10%. In this case also, age is a factor. The death rate among treated patients under 20 years of age is about 1%, but the rate rises with age to over 15% in patients over 50. The mortality rate of patients with type III infections treated with penicillin is about 12%. With present forms of medication it is unlikely that the rate will be lowered

TABLE IV

SUMMARY OF CHARACTERISTICS OF COMMONLY ENCOUNTERED SPECIFIC FORMS OF PNEUMONIA

Cause	*Pneumococcus*	*Hemolytic streptococcus*	*Klebsiella*	*Influenza Bacillus*	*Staphylococcus aureus*	*Adenoviruses, influenza viruses, etc*
Percentage of acute Pneumonias in adults	98%	0 9%	0 6%	0 3%	0 1%	Indeterminable, exceed all other forms
Predisposing Factors	Minor infections of respiratory tract	Minor infections of respiratory tract Streptococcic pharyngitis Influenza	Senility, or debilitation other chronic pulmonary disease	Infancy childhood chronic lung disease Influenza	Minor infections of respiratory tract, especially influenza	During epidemics of mild respiratory tract infections or sporadic
Onset and Symptoms	Sudden chill fever cough rusty sputum pain in chest	Sore throat Gradual or sudden cyanosis irregular fever	Often sudden as in pneumococcus Often severe	Often sudden cough dyspnea cyanosis	Gradual or sudden chill or chills remittent fever sweating	Sudden or gradual mild symptoms gradually worsen chilliness sweating, bradycardia, usually mild, often unrecognized
Pulmonary Signs	Signs of sequence of congestion, consolidation and resolution	Patchy areas of pneumonic involvement Pleural effusion common	Patchy areas of pneumonia often signs of consolidation later abscess and cavitation	Inflammation upper airways patchy pneumonia	Patchy areas of pneumonic involvement later of abscess and cavitation	Minimal in contrast with roentgenographic changes Patchy pneumonic areas
Sputum	Tough rusty contains causative pneumococci	Uncharacteristic often thin mucopurulent blood tinged Streptococci present	Bloody mucoid Klebsiella in large numbers Hemoptysis	Blood tinged mucopurulent contains H influenzae	Uncharacteristic purulent, predominance of staphylococci	Scanty uncharacteristic Sparse bacteria often contains monocytes
Leukocyte Count	Leukocytosis polymorphonuclear	Variable usually polymorphonuclear leukocytosis	Variable usually polymorphonuclear leukocytosis	Usually leukopenia later leukocytosis	Variable usually polymorphonuclear leukocytosis	Usually normal low leukocytosis later occasionally monocytosis
Roentgenography	Uniform lobar density	Diffuse patchy pneumonic areas Pleural effusion	Patchy consolidation later abscess cavitation and fibrosis in chronic form	Diffuse patchy pneumonia	Peribronchial patchy densities later confluent with abscess and cavitation	Soft scattered densities out of proportion to sparse physical signs Areas of atelectasis
Therapy of Choice	Penicillin Tetracyclines Chloramphenicol Erythromycin	Same as for Pneumococcus Aspiration of pleural fluid	Streptomycin Sulfadiazine Tetracyclines Chloramphenicol	Same as for Klebsiella	Penicillin Erythromycin Novobiocin Vancomycin	
Serious Accompanying Conditions or Sequels	Empyema Endocarditis Meningitis	Empyema	Multiple lung abscess hemoptysis later cavitation or chronic disease	Suffocation hemoptysis abscess	Multiple abscesses in lung empyema cysts	Rarely complicated Circulatory collapse

quired or the intercostal nerves of the painful area may be injected with a small amount of 1% solution of procaine

Abdominal distention rarely occurs during modern therapy It is controlled by removing from the diet milk sugar or vegetables apt to cause excessive formation of gas The bowels if constipated may be aided by a mild laxative an enema or by changing the diet Distention itself may be hard to reduce The application of heat in the form of stupes is traditional but the use of plastic or rubber suction tubes inserted orally or rectally according to where the gas collects may serve to remove it

For dyspnea and cyanosis the patient may be placed in a tent in an oxygen saturation of at least 60% or he may be given oxygen by means of a face mask or nasal catheter The most serious occurrence is circulatory collapse or a shock like state which often resists treatment The best treatment is the control of the infection itself Maintaining the body temperature near 37°C (98 6°F) by heat applied with warm blankets is helpful The intravenous injection of isotonic solution of sodium chloride or of plasma may be tried but the problem is not so much one of supplying fluid as of favoring its circulation Norepinephrine and related compounds may aid in sustaining the blood pressure over the critical period Digitalis is of no value except in the presence of auricular fibrillation or actual heart failure The so called cardiac stimulants like coramine adrenalin caffeine and strychnine are useless or may be harmful Morphine is contraindicated Atropine does not control pulmonary edema but venesection may be helpful in plethoric patients

TREATMENT WITH HYDROCORTISONE

In a series of 52 patients treated with penicillin and hydrocortisone recovery occurred within 24 hours in all but 2 The symptoms improved rapidly but persisted almost as long as in patients who did not receive the hormone No harmful effects were noted The procedure still is in the trial stage The dosage was 80 mg initially then at 6 hour intervals 60 mg for three doses 40 mg for four doses 20 mg for four doses 10 mg for four doses and finally 10 mg every 12 hours for two doses

ANTIMICROBIC THERAPY

Specimens of sputum and blood for identification of the bacteria should be taken before drug therapy is started In many instances treatment must be given before bacteriologic data are ready When the diagnosis of pneumococcic pneumonia is made clinically penicillin should be given promptly Several methods are in vogue but the following are preferable at present In the case of average severity treated early in the disease 200 000 units (120 mg) of aqueous crystalline penicillin are injected intramuscularly as an initial dose after which 100 000 units (60 mg) are given every 12 hours until recovery occurs (Fig 8) This dosage may be maintained or reduced in amount for 24 to 48 hours afterward In severe cases in patients with complications if treatment is not begun until several days have elapsed or if other reasons demand an initial dose of from 200 000 to 400 000 units (120 to 240 mg) may be given intravenously and followed by 200 000 units (120 mg) or more intramuscularly every 12 hours (Figs 9 and 11) Many authorities recommend twice or thrice these amounts which seem excessive for most cases Others recommend a combination of quick acting and repository preparations of penicillin

Penicillin V given orally may give results as good as those after intramuscular injection but the uncertainty of absorption must be considered Penicillin if given orally should be in triple the amounts given intramuscularly in divided doses at intervals of every 3 or 4 hours The amount of penicillin which reaches the infected tissue is of far greater importance than the amount present in the blood

If a patient is known to be hypersensitive to penicillin or if evidence of hypersensitivity appears time does not permit the uncertain procedure of desensitization It is better to substitute erythromycin tetracycline or sulfadiazine

If no favorable response to penicillin occurs the dosage is insufficient an error in diagno-

further Delayed or insufficient treatment, errors, other disease, old age, multilobar involvement, and other factors account for most of the deaths at present

Relapse of pneumonia may occur in patients insufficiently treated or when treatment is stopped too soon

COMPLICATIONS

This chapter pertains to pneumonia and only brief mention is made of extrapulmonary complications Pleural effusion of some degree occurs whenever the pleura is involved Large amounts rarely occur, but it must be known whether the fluid is infected (empyema) or not If not, it usually is resorbed and needs no treatment Atelectasis occasionally occurs (see empyema, page 152)

Purulent complications occur in from 3 to 11% of cases depending upon the adequacy of early treatment Purulent localization may begin before treatment is started Empyema is the most important Others are pericarditis, endocarditis, meningitis, arthritis, otitis media, mastoiditis, sinusitis and peritonitis Abscess of the lung is rare but occasionally occurs in prolonged disease caused by type III pneumococci Other bacteria, especially hemolytic streptococci or staphylococci occasionally cause complicating infections

Circulatory failure is a serious complication which often resists correction

PREVENTION

There are no reliable practicable measures to prevent pneumonia It would be most logical to prevent minor respiratory tract infections which precede pneumonia so often Some progress has been made in the development of vaccines against influenza and infections caused by adenoviruses of types 3 4 and 7 Ultraviolet irradiation of the air or the use of virucidal or bactericidal aerosols have not been effective

No evidence favors the routine practice of giving antimicrobics to patients with colds to prevent pneumonia Exception may be made in persons in whom pneumonia would be especially dangerous, as for example, during pregnancy, in old people or in those with other disease and for surgical patients

Vaccines prepared with the pneumococcic polysaccharides apparently have some value in preventing pneumonia but are strictly specific type for type[5] Their general use is not recommended Under certain conditions such as an outbreak of pneumonia in a closed group, vaccines may be effective

MANAGEMENT OF PNEUMONIA

Since antimicrobic therapy limits pneumococcic pneumonia to a disease of short duration, the need for symptomatic therapy is not so great as formerly Unless illness lasts more than a day or two, no special attention need be given to the diet, fluid intake and elimination if they are sufficient

Cough may be eased by mentholated lozenges, by humidifying the air or by the inhalation of steam from a vaporizer If cough is harassing and exhausting, codeine sulfate in doses of 15 to 60 mg (1/4 to 1 grain) orally may be given every 3 or 4 hours Morphine rarely is required Coughing should not be suppressed entirely Expectorant drugs and cough syrups are useless, they disturb digestion and should not be given They do not aid in liquefying sputum nor in increasing its amount

Thoracic pain may be controlled by the application of a many-tailed flannel binder, tightened and pinned to suit the patient's comfort Heat applied locally is helpful In severe cases, codeine or morphine may be re

quired or the intercostal nerves of the painful area may be injected with a small amount of 1% solution of procaine

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sis was made or some complicating secondary infection or condition is present The reason should be sought and if necessary other treatment added or substituted

With proper therapy the temperature usually falls to normal and recovery occurs after 24 to 36 hours (Fig 8) Occasionally several days may be required (Fig 9) If improvement does not occur if the pneumonia spreads or if extrapulmonary purulent localization is present *the dosage should be increased* (Figs 10 and 11) Therapy may be tapered off and discontinued after the fever has been below 37 2°C (100°F) for 2 or 3 days Should relapse occur therapy must be resumed Fever caused by penicillin itself must be considered

OTHER EFFECTIVE ANTIMICROBIC AGENTS

If penicillin causes undesired side effects if the response to therapy is unsatisfactory if penicillin has controlled the pneumococcic *infection and another penicillin resistant* bacterium becomes invasive or if mixed infection with penicillin resistant bacteria is present recourse may be had to other agents Erythromycin tetracycline drugs novobiocin or chloramphenicol may be given orally in doses of 1 to 3 gm daily in divided amounts They may be given intravenously in doses of 0 5 *to 1 0 gm every 12 hours At times they* cause unpleasant gastrointestinal or other disturbance or provoke superinfection with antimicrobic resistant bacteria [7 9]

SULFADIAZINE

An advantage of sulfadiazine or sulfamerazine over other agents is their low cost Both are effective when used orally or parenterally but because of their frequent toxic effects they have been replaced almost entirely If the antimicrobics mentioned are unavailable *or if other reasons* prevent their use sulfadiazine may be used Oral dosage of 2 to 4 gm initially followed by 1 gm every 4 or 6 hours is the rule Al[illegible] cc *of fluid* a day should be given [illegible] the formation of crystals in th[illegible] The urine should be kept alkali[illegible] 15 to 30 gm of sodium bicarb[illegible] divided doses In severe cases [illegible] rapy is not [illegible] sodium [illegible] d be give[illegible] ously To [illegible] be inti[illegible] l *if they* must

ISOLATION OF PATIENTS

Most bacterial pneumonias are not highly contagious but the occasional occurrence of multiple cases in a community indicates the need for caution Strict isolation is not necessary *but the patient should be instructed* to cough into a gauze pad Sputum should be disinfected or burned and eating utensils should be washed in hot soapy water

EMPYEMA

Empyema responds best to treatment in the early stage before the exudate thickens or adhesions form The pus should be aspirated and 100 000 units (60 mg) of crystalline penicillin in water *injected into the pleural space* Intramuscular injections of the drug should be continued as for the pneumonia Intrapleural injection may be repeated daily or every other day for a week or more If the pus becomes thick or if improvement does not occur by then thoracotomy and drainage is indicated Intrapleural injection of strepto*dornase streptokinase or trypsin* may aid in di[illegible] fibrin but must be carefully used ([illegible] r 22)

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OTHER BACTERIAL PNEUMONIAS

As indicated in Table III bacteria other than the pneumococcus are relatively rare causes of pneumonia The most important ones are group A beta hemolytic streptococci Klebsiella (Friedlander's bacilli) H influenzae (Pfeiffer's bacilli), and micrococci (staphylococci) in about that order These are invasive when the resistance of pulmonary tissue is weakened by minor viral infections or other factors Depending on the prevalence of minor viral infections and on the kind of bacteria dominant in a community isolated cases or small epidemics of bacterial pneumonias may occur During the pandemic of influenza in 1918, the bacteria named either singly or in combinations caused most of the fatal pneumonias

Meningococci gonococci nonhemolytic streptococci and M tetragenus are still rarer causes The lungs at times are involved during systemic disease caused by Past tularensis Past pestis Brucella S typhosa and Shigella Pneumonias secondary to a variety of mechanical or other disturbances like congestion aspiration and atelectasis usually are associated with a mixture of bacteria any one or several of which may be operative

HEMOLYTIC STREPTOCOCCIC PNEUMONIA

As shown in Table III streptococci are not a common cause of pneumonia Most cases are encountered as secondary infections during epidemics of measles influenza or other viral infections of the respiratory tract They may accompany scarlet fever streptococcic sore throat or erysipelas Sporadic cases occur

Clinically the onset may be obscured by the predisposing infections just named The early period is characterized by chilliness or a chill and an intensification of the preceding illness Fever rises to higher levels there are cough pain in the chest prostration and tachycardia Several lobes or both lungs may be affected The sputum is variable but often is thin and bloody In severe cases dyspnea and cyanosis occur The leukocytes may be normal or increased in number Bacteremia is not common Empyema occurs but differs from that in other pneumonias by its early appearance and a characteristic infected serosanguineous massive effusion Fluid tends to reaccumulate rapidly if it is aspirated

The disease may last two or three weeks and recovery is gradual The mortality rate during serious epidemics of influenza and measles and before the advent of antimicrobic drugs was reported as between 35 and 60% The disease is said to favor residual bronchiectasis emphysema or fibrosis but the evidence therefor is not established

Diagnosis

The presence of influenza measles or hemolytic streptococcic sore throat is of aid in diagnosis Diagnosis can be made with certainty by the demonstration of hemolytic streptococci in predominance in the sputum or in pure culture from the blood pleural exudate or lung The antistreptolysin titer in

sis was made, or some complicating secondary infection or condition is present The reason should be sought, and, if necessary other treatment added or substituted

With proper therapy the temperature usually falls to normal and recovery occurs after 24 to 36 hours (Fig 8) Occasionally several days may be required (Fig 9) If improvement does not occur, if the pneumonia spreads or if extrapulmonary purulent localization is present, the dosage should be increased (Figs 10 and 11) Therapy may be tapered off and discontinued after the fever has been below 37 2°C (100°F) for 2 or 3 days Should relapse occur, therapy must be resumed Fever caused by penicillin itself must be considered

OTHER EFFECTIVE ANTIMICROBIC AGENTS

If penicillin causes undesired side effects, if the response to therapy is unsatisfactory, if penicillin has controlled the pneumococcic infection and another penicillin-resistant bacterium becomes invasive, or if mixed infection with penicillin-resistant bacteria is present, recourse may be had to other agents Erythromycin, tetracycline drugs, novobiocin or chloramphenicol may be given orally in doses of 1 to 3 gm daily in divided amounts They may be given intravenously in doses of 0 5 to 1 0 gm every 12 hours At times they cause unpleasant gastrointestinal or other disturbance, or provoke superinfection with antimicrobic resistant bacteria[7-9]

SULFADIAZINE

An advantage of sulfadiazine or sulfamerazine over other agents is their low cost Both are effective when used orally or parenterally but because of their frequent toxic effects, they have been replaced almost entirely If the antimicrobics mentioned are unavailable or if other reasons prevent their use, sulfadiazine may be used Oral dosage of 2 to 4 gm initially followed by 1 gm every 4 or 6 hours is the rule About 1500 cc of fluid a day should be given to minimize the formation of crystals in the kidneys The urine should be kept alkaline by giving 15 to 30 gm of sodium bicarbonate daily in divided doses In severe cases or if oral therapy is not possible, sodium sulfadiazine should be given intravenously Toxic effects must be anticipated and if they are severe, therapy must be stopped

ISOLATION OF PATIENTS

Most bacterial pneumonias are not highly contagious, but the occasional occurrence of multiple cases in a community indicates the need for caution Strict isolation is not necessary but the patient should be instructed to cough into a gauze pad Sputum should be disinfected or burned, and eating utensils should be washed in hot, soapy water

EMPYEMA

Empyema responds best to treatment in the early stage before the exudate thickens or adhesions form The pus should be aspirated and 100 000 units (60 mg) of crystalline penicillin in water injected into the pleural space Intramuscular injections of the drug should be continued as for the pneumonia Intrapleural injection may be repeated daily or every other day for a week or more If the pus becomes thick or if improvement does not occur by then thoracotomy and drainage is indicated Intrapleural injection of streptodornase, streptokinase or trypsin may aid in dissolving fibrin, but must be carefully used[10] (see Chapter 22)

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OTHER BACTERIAL PNEUMONIAS

As indicated in Table III bacteria other than the pneumococcus are relatively rare causes of pneumonia The most important ones are group A beta hemolytic streptococci Klebsiella (Friedlander's bacilli) H influenzae (Pfeiffer's bacilli) and micrococci (staphylococci) in about that order These are invasive when the resistance of pulmonary tissue is weakened by minor viral infections or other factors Depending on the prevalence of minor viral infections and on the kind of bacteria dominant in a community isolated cases or small epidemics of bacterial pneumonias may occur During the pandemic of influenza in 1918 the bacteria named either singly or in combinations caused most of the fatal pneumonias

Meningococci gonococci nonhemolytic streptococci and M tetragenus are still rarer causes The lungs at times are involved during systemic disease caused by Past tularensis Past pestis Brucella S typhosa and Shigella Pneumonias secondary to a variety of mechanical or other disturbances like congestion aspiration and atelectasis usually are associated with a mixture of bacteria any one or several of which may be operative

HEMOLYTIC STREPTOCOCCIC PNEUMONIA

As shown in Table III streptococci are not a common cause of pneumonia Most cases are encountered as secondary infections during epidemics of measles influenza or other viral infections of the respiratory tract They may accompany scarlet fever streptococcic sore throat or erysipelas Sporadic cases occur

Clinically the onset may be obscured by the predisposing infections just named The early period is characterized by chilliness or a chill and an intensification of the preceding illness Fever rises to higher levels there are cough pain in the chest prostration and tachycardia Several lobes or both lungs may be affected The sputum is variable but often is thin and bloody In severe cases dyspnea and cyanosis occur The leukocytes may be normal or increased in number Bacteremia is not common Empyema occurs but differs from that in other pneumonias by its early appearance and a characteristic infected serosanguineous massive effusion Fluid tends to reaccumulate rapidly if it is aspirated

The disease may last two or three weeks and recovery is gradual The mortality rate during serious epidemics of influenza and measles and before the advent of antimicrobic drugs was reported as between 35 and 60% The disease is said to favor residual bronchiectasis emphysema or fibrosis but the evidence therefor is not established

Diagnosis

The presence of influenza measles or hemolytic streptococcic sore throat is of aid in diagnosis Diagnosis can be made with certainty by the demonstration of hemolytic streptococci in predominance in the sputum or in pure culture from the blood pleural exudate or lung The antistreptolysin titer in

the blood often reaches a high level. Hemolytic streptococci may be found as secondary invaders in pneumonia caused by other bacteria.

Treatment

Treatment with penicillin or sulfadiazine has not given results as striking as those obtained in pneumococcic pneumonia, yet they are the therapeutic agents of choice. Parenteral injection is recommended. The methods of treatment of streptococcic pneumonia and empyema are the same as those outlined on page 150. Tetracycline drugs and chloramphenicol also have been used with success in a few cases.

Antimicrobics given prophylactically during virial infections do not serve to prevent streptococcic pneumonia.

STAPHYLOCOCCIC PNEUMONIA

Staphylococci are prominent among the bacteria normally present in the oropharynx, yet they rarely invade the lung. They account for about 0.1 per cent of bacterial pneumonias. The incidence may increase with the increased prevalence of antimicrobic resistant staphylococci noted in the past few years. As in the case of other pathogens, invasion is favored by factors which reduce resistance. Staphylococcic pneumonia usually is secondary to some viral infection of the respiratory tract, but also occurs in debilitated persons, especially in infants.[1] Many of the cases described were observed during epidemics of influenza.[2,3] Staphylococci may become invasive during therapy with broad spectrum antimicrobics. Staphylococcus aureus is the chief cause, but Staph. albus occasionally is present alone. Blood borne metastatic staphylococcic infection of the lung gives rise to multiple infected pulmonary emboli or infarcts and early formation of abscesses.

Pathology

Pathologically the lesion resembles that caused by staphylococci in other tissues: The pneumonic areas are patchy and scattered. Consolidation, if it occurs, is not as firm as in pneumococcic pneumonia. In the acute stage a suppurative necrotizing inflammatory process affects the bronchi, bronchioles, adjacent alveolar tissue and septums. There are hemorrhage, edema, polymorphonuclear cell exudate and formation of miliary abscesses. As the process evolves, small abscesses coalesce to form larger ones. Large clumps of staphylococci are present. The lesions may heal with no trace or become fibrotic. Large cavities may result, some filled with pus, others empty as thin walled cysts.

Symptoms

It may be difficult to date the onset of pneumonia if a minor respiratory tract infection precedes the disease. When pneumonia begins there may be chilliness or chills, and the illness increases in intensity. Fever rises higher and becomes remittent or irregular, characteristic of staphylococcic infection. In the early period the signs and symptoms may be uncharacteristic and resemble other kinds of pneumonia. Tachycardia, sweating and pain in the chest occur. The sputum usually is purulent and streaked with blood. In fulminating cases symptoms intensify with alarming speed. Pulmonary edema, pallor, cyanosis and a shock like state suggestive of a violent toxemia may end in death in a day. In the milder case the disease, if untreated, lasts for two to four weeks or more and the remittent temperature falls by lysis. If the disease progresses and abscess formation proceeds, the purulent sputum may increase or may first appear in large amount if the abscesses break through and discharge into the bronchi. Broncho-pleural fistula may occur. Signs of cavitation and later of large cysts may be present. Recovery may be complete, or chronic abscesses may remain. With healing, the area may become fibrotic or large thin walled cysts may form. Empyema occurs more often in infants than in adults.

There may be leukopenia, a normal count or leukocytosis. The sputum almost always is purulent and contains great numbers of staphylococci. The blood stream is invaded in about 25% of cases. Roentgenograms show scattered areas of infiltration in one or both lungs. In the later stage single or multiple

purified areas of cavitation with or without fluid levels may be present

The mortality rate in untreated patients is estimated as 50% but probably is much less Treatment with antimicrobics improves the prognosis but not to the degree as in pneumococcic pneumonia

Diagnosis

Diagnosis depends chiefly on the demonstration of large numbers of staphylococci in the sputum and their presence in the blood or in purulent localizations High irregular or remittent fever toxemia and the development of multiple abscesses and cavities in the lung are characteristic features

Treatment

Treatment is the same as for other severe staphylococcic infections Penicillin once was the therapeutic agent of choice but the unfortunate development of many penicillin resistant strains has reduced its value If the cocci are sensitive penicillin in large amounts 300 000 units (180 mg) to 1 000 000 units (600 mg) or more should be given intramuscularly every 12 hours For resistant strains erythromycin novobiocin vancomycin bacitracin tetracycline or chloramphenicol may be substituted in appropriate dosage according to the indication of tests for sensitivity The intensity and duration of treatment depend upon the clinical response Therapy is not as effective as in pneumococcic pneumonia Observations on the value of adrenocorticotropic hormones to reduce the severity of symptoms have not yet been reported Empyema if present should be treated according to instructions given on Chapter 22

PNEUMONIAS CAUSED BY OTHER COCCI

These are rarities Nonhemolytic streptococci are reported as causes of pneumonia at times on rather weak evidence *Gaffkya tetragena* causes pneumonia indistinguishable clinically from staphylococcic infection *Neisseria* of catarrhalis gonococcic and meningococcic varieties may cause specific pulmonary infection Sporadic cases[4] and small outbreaks of pneumonia caused by *meningococci* were observed during epidemics of meningitis The symptoms and signs are uncharacteristic and diagnosis is aided by the presence of an epidemic and proved by isolation and identification of the meningococcus The mortality rate is high in untreated cases Penicillin or sulfadiazine are effective in therapy

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KLEBSIELLA PNEUMONIAE (FRIEDLANDERS BACILLUS) PNEUMONIA

This constitutes less than 1 of all pneumonias It usually is sporadic but small epidemics have been observed Over 70% of cases occur in persons over 50 years of age Chronic alcoholism malnutrition and debility are predisposing factors In young persons minor respiratory tract infections may incite the disease The bacilli may be secondary invaders during pneumonia of other origin and the reverse may occur

There are many serologic types of Kl pneumoniae of which Types A and B are the most important The pulmonary lesion often is massively lobar or lobular with plaques of fibrin on the adjacent pleura The cut surface is mottled red brown covered with a thick stringy exudate containing pus erythrocytes and large gram negative capsulated bacilli Abscesses are present in old lesions The alveolar tissue is necrotic and many bacilli are there

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Treatment

Treatment with penicillin or sulfadiazine has not given results as striking as those obtained in pneumococcic pneumonia yet they are the therapeutic agents of choice Parenteral injection is recommended The methods of treatment of streptococcic pneumonia and empyema are the same as those outlined on page 150 Tetracycline drugs and chloramphenicol also have been used with success in a few cases

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Pathology

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Symptoms

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Treatment

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Symptoms

The *onset of the disease is much like that* of pneumococcic lobar pneumonia It often is sudden with a chill, pain in the chest, cough, sputum, vomiting and diarrhea Hemoptysis or gelatinous bloody sputum is an important feature Prostration, headache, delirium and abdominal distention commonly occur Fever may not rise to high levels and tends to be remittent In aged patients the fever may be low or absent owing to poor reaction to infection It may rise to high levels *from time* to time if the infection spreads to other parts of the lung Tachycardia, dyspnea, cyanosis and jaundice may occur Bacteremia occurs in 70% of patients The disease in some instances passes into the chronic stage [1]

The mortality rate in young persons is low, *in those over 50 who are untreated it is from* 70 to 80% In one group of patients about 50% died, 16% recovered, and in 33% the disease progressed into the chronic stage Antimicrobic therapy is said to reduce the death rate to 40%

The physical signs may be characteristic of consolidation, but are less pronounced and are scattered in patches in both lungs More often there are dullness, suppressed breath and voice sounds and fine and coarse rales In protracted cases, evidence of suppuration may appear, but unless an abscess is evacuated, signs of cavitation may not be present *Roentgenographic shadows show dense areas* of infiltration, consolidation, and later if cavitation occurs, of rarefied areas or multiple thin-walled cavities with or without fluid Permanent fibrosis and scarring with cavitation, distortion of the mediastinum and thickened pleura may follow

Chronic Form

In patients who survive the acute attack, *infection may persist for years* like tuberculosis It is characterized by low irregular fever with remissions and exacerbations, tachycardia, dyspnea, cyanosis, sweating, cough, hemoptysis, sputum and emaciation Bronchiectasis, abscesses, necrosis, cavitation, pleural effusion, empyema and fibrosis result In one recorded instance, the disease lasted 9 years

Diagnosis

An acute pneumonia in an elderly or debilitated person in which the signs are confined to one or more lobes and which is not pneumococcic in origin *should suggest the diagnosis* The characteristic bloody, mucinous, stringy sputum containing a predominance of large, capsulated gram negative bacilli almost completes it Proof is obtained by identifying and typing K1 pneumoniae obtained from the sputum, exudate or blood The leukocytes *often are normal in number but may rise to* 20 000 especially during exacerbation or when purulent localization occurs There may be leukopenia

In differential diagnosis, pneumococcic, staphylococcic and tuberculous pneumonia must be ruled out in the acute phase, and *pulmonary tuberculosis, chronic lung abscess* and bronchiectasis in protracted cases

Treatment

Specific treatment is not as effective as in certain other pneumonias Victims often are senile, alcoholic or are otherwise debilitated and require special supportive management for these defects K1 pneumoniae are sensitive to the tetracyclines, to chloramphenicol *and to streptomycin* [2] *Penicillin and the sul*fonamides seldom are effective At present, a combination of streptomycin and either a tetracycline drug or chloramphenicol seems to be the best form of treatment A tetracycline alone may be given in doses of 0 5 gm every 4 to 6 hours orally, but tetracycline, as stated *in combination with streptomycin* in doses of 0 5 gm intramuscularly every 6 hours may be better In severe cases, tetracycline given intravenously instead of orally, 0 5 gm every 4 to 6 hours is recommended Response to therapy often is slow In one series of 22 treated patients 9 died [3] The value of cortisone for severe disease has not been reported on

Focal purulent complications should be sought and drained For empyema, streptomycin may be *injected intrapleurally* in amounts of 5 to 100 mg in dilution of 1 to 10 mg per cc of isotonic solution of sodium chloride Surgical drainage may be necessary

For chronic pneumonia and abscess formation lobectomy has been performed with success

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HEMOPHILUS INFLUENZAE PNEUMONIA

True influenzal pneumonia is caused by the viruses of influenza (page 134) The misnamed bacillus H influenzae (Pfeiffer's bacillus) as a secondary invader may cause pneumonia during viral respiratory tract infections or other disease Type b H influenzae is the chief cause especially in childhood Pathologically there are no distinctive features of the pneumonia except for the presence of H influenzae The cellular reaction is chiefly monocytic and interstitial tissue is involved Tracheitis pleuritis and sinusitis may be present

Symptoms

There are no clinical features to distinguish H influenzae pneumonia from other forms of patchy pneumonia It is preceded often by a minor viral infection of the respiratory tract The severity varies greatly depending on the age and condition of the patient and on the gravity of the predisposing infection Fever is apt to be high and irregular tending to rise and fall as the process spreads from place to place Cough dyspnea cyanosis and pleural pain are common The sputum is purulent often bloody and may contain great numbers of H influenzae Bacteremia is rare The leukocytes vary in number from 2 000 to 20 000 Purulent empyema rarely occurs The physical signs are those of patchy migratory pneumonia Modified signs of consolidation may be elicited over areas of confluence of pneumonic patches The course lasts one to several weeks It is believed by some that the involvement of interstitial tissue may lead to emphysema fibrosis or bronchiectasis

Specific diagnosis depends on the isolation and identification of H influenzae in large numbers from the sputum, and occasionally from the blood or purulent exudate

Treatment

Sulfadiazine once was used with some success At present three agents streptomycin tetracycline and chloramphenicol are said to be effective Streptomycin is given in amounts of 2 to 3 gm daily intramuscularly until fever disappears and in reduced dosage for several more days[1] Some observers recommend streptomycin combined with sulfadiazine Tetracycline drugs or chloramphenicol are given orally or parenterally in doses of 2 to 4 gm daily in a similar manner

HEMOPHILUS PERTUSSIS PNEUMONIA

Whooping cough ordinarily is considered primarily as an infection of the upper respiratory tract and bronchial tree but the lungs are involved in a pneumonic process as shown roentgenographically in from 50 to 80% of cases particularly in infants Clinical evidence of pneumonia occurs in a smaller number Because whooping cough is a relatively common disease among infants and children the pneumonia incident thereto is more common than many other kinds of pneumonia but is disregarded or overlooked and seldom included in statistics of pneumonia In most instances H pertussis is the cause but pneumococci streptococci and other bacteria may be secondary invaders When pneumonia is prominent there is tachycardia tachypnea and dyspnea with rhythmic flaring of the alae nasi The pulmonary physical signs of pneumonia are variable sometimes absent Transient areas of dullness bronchial breathing and rales may be observed Coughing becomes more frequent but less paroxysmal Pleural effusion may occur There often is lymphocytosis and the sputum contains H pertussis Pathologically the trachea bronchi and bronchioles are inflamed show petechial hemor

rhages and contain mucus or mucopus. The pneumonic areas are associated with the bronchioles in patchy distribution. Microscopically the lesion is chiefly an interstitial one with a monocytic infiltration like that of viral infections. In later stages other bacteria and the results of their pathogenicity are found. Some observers believe that whooping cough and the pulmonary lesions which accompany it are the precursors of chronic pulmonary disease like bronchiectasis, emphysema or fibrosis but the evidence is not convincing.

The prognosis depends much upon the age of the patient. In infants less than a year old the mortality rate ranged from 25 to 40%, most of the fatal cases were pneumonic. Modern therapy has reduced the death rate to 2.4% in young infants and to 0.4% in those over 2 years of age.

Treatment

The management of pertussis itself is not discussed here. At present chloramphenicol or the tetracycline drugs are recommended. Streptomycin also is said to be of value. For pneumonia caused by secondary infection the appropriate antimicrobic or combination of antimicrobics must be selected according to the sensitivity of the invading bacteria. The symptomatic treatment is the same as for Viral pneumonia as outlined in page 133.

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MYCOBACTERIUM TUBERCULOSIS PNEUMONIA (See Chapter 8)

PASTEURELLA TULARENSIS PNEUMONIA

(Tularemic Pneumonia)

Tularemia is an acute infectious disease primarily of animals and birds but is transmissible to man. It is caused by Pasteurella tularensis, an organism related to P. pestis. The general behavior of tularemia, except in severity, is much like that of plague and is not discussed here. It is estimated that 50% or more of persons with tularemia show evidence of localization of the infection in the lung, in most instances as a metastatic lesion occurring with others or rarely as the primary pneumonic form in which the bacilli presumably gained entrance through the mucous membranes of the bronchi and lungs.

Incidence

The reported incidence of tularemia in the United States in 1954 was 681 cases and many more no doubt occur. If as estimated about 50% of patients have pulmonary involvement about 350 cases of the pneumonic form occurred, but in many patients there is no clinical evidence of pneumonia. Pulmonary symptoms are prominent enough to suggest pneumonia in 10 or 20% of cases. Most of the cases develop during the hunting season when human contact with the wild rabbits is greatly increased. West of the Mississippi River the disease is most common in the summer months when deer flies and ticks are most active.

Pathogenesis

The bacilli of tularemia gain entrance into the body by the routes already mentioned. The lungs usually are invaded by way of the blood stream and pneumonia occurs as a concomitant localization. In the rare primary pulmonic form, as in plague, infection apparently is acquired by inhaling bacilli suspended in the air as dust or in droplets expelled from patients or animals who have tularemic pneumonia or from handling dried cultures of the bacteria.

Pathology

The characteristic pathologic features are the ulcer at the site of infection and areas of focal necrosis in the affected lymph nodes, liver, spleen and lungs. Many patients whose lungs or pleurae are involved recover, but in most fatal cases studied at necropsy pneu

monia or pleuritis is present. In one group of collected reports of necropsy studies pulmonary or pleural lesions were found in 73 %.[1] Pleural effusion was noted in 50%.

The most frequent pulmonary lesion in fatal cases is a nodular or confluent form of pneumonia involving a single lobe, several lobes or all of the lobes. The usual phases of red and gray hepatization occur. Central whitish or yellowish necrosis often is found in the gray areas. The cut surface shows small or large areas of coagulative or caseous necrosis. Occasional scattered small interseptal areas of focal necrosis are found. In advanced cases cavities may be present resembling those of chronic pulmonary tuberculosis. The exudate is composed chiefly of mononuclear cells. When secondary infection with various cocci is present, many polymorphonuclear leukocytes are found. The alveolar septums usually are congested, especially in the pneumonic areas, and frequently the walls are necrotic. Interstitial infiltration by lymphocytes, mononuclear and other cells is not prominent in most cases and may be confined to the interlobar septums, peribronchial and perivascular tissues. P. tularensis seldom is demonstrable in the lesions even when bacilli can be cultivated from the same portion of the lung.

Symptoms

References to numerous isolated case reports of pneumonia occurring in tularemia are given elsewhere.[3] In a series of 35 cases Blackford found evidence of pneumonia in seven, of bronchitis in 7 and of pleural effusion in 3. Clinical evidence of pleural, bronchial or pulmonary involvement was present therefore in about half of his cases, and roentgenographic evidence of abnormalities in the chest was found in the majority of patients, most of whom recovered.

The Primary Form

In 7 of 16 cases of Kavanaugh's series the infection appeared to originate as a primary pneumonia, suggesting that infection entered through the respiratory tract. In 4 of these cases some other member of the family had cutaneous tularemia. The onset may be abrupt with a chill, fever, dyspnea, cough, pain in the chest and sweating. Cough and sputum appear early. No other signs such as lymph node enlargement may be found. The spleen may become palpable later.

The Secondary Form

The onset of pneumonic symptoms in ulceroglandular tularemia may occur from 2 days to many months after the systemic infection begins. Seven of eight patients studied by Kavanaugh with the typhoid type also had serious pulmonary disease.

The pulmonary symptoms vary greatly in severity and often are so mild that pneumonia cannot be recognized without roentgenographic aid. Symptoms of bronchitis usually precede pneumonia. Cough usually is present and may develop gradually. The sputum may be absent or profuse and bloody. Pain in the chest may occur. The fever is irregular and the pulse rate relatively slow. Tachypnea, drowsiness, stupor and cyanosis are present only in the most severe cases. The leukocyte count is usually within normal limits. The symptoms and signs of pneumonia may be transient or may last for weeks, occasionally ending in pulmonary abscess, cavitation or permanent fibrosis, especially when secondary infection with other bacteria occurs.

The physical signs of both primary and secondary forms are uncharacteristic. Both lungs frequently are involved. Patchy areas of consolidation are indicated by the irregular distribution of small areas where rales, harsh breath sounds and weak bronchophony are heard. The location of the signs may vary from day to day. Confluent areas yield signs of consolidation with bronchial breath and voice sounds and dullness. Cavities may be detected in protracted cases. Roentgenographic studies during tularemia are of importance since pneumonia may not be detected by physical examination. Residual changes of fibrosis are found in many cases. The subject was discussed by Bibbs and Berland.[2]

Prognosis

Tularemic pneumonia may be trivial, transient and unnoted save for roentgenographic evidence. In other cases it may be the cause of death. The duration of the pneumonia is

variable It may last from a few days to several weeks Too few cases thus far have been recorded to estimate the mortality rate when pneumonia is present and if the patient receives no antimicrobial therapy, but it probably lies between 10 and 25% Appropriate treatment usually terminates the disease in a day or two If pulmonary signs persist after this time they probably indicate abscess formation, fibrosis or secondary infection

Diagnosis

During tularemia an increase in the pulse rate, respiratory rate, fever and the appearance of cough and sputum suggest pulmonary invasion But it still is not possible to be certain whether the pulmonary lesion is tularemic in nature or caused by other secondarily invading bacteria unless P tularensis can be demonstrated in the sputum, in material removed from the lung by lung puncture and aspiration, by finding the bacilli in the pleural exudate, or by postmortem examination The nature of changes shown by the roentgenogram is not pathognostic

Diagnosis is difficult when pneumonia occurs in the *typhoid form of tularemia* or when the infection appears to be primary in the lung Under these circumstances a *history of contact with a probable source of infection* is important The clinical course with evidence of pneumonia softening or cavity formation and a low leukocyte count may be helpful Puzzling skin eruptions may occur If the patient is observed from the onset, a temporary remission of the temperature may occur after the first day or two Diagnosis is established by cultivating the organism from the blood on special medium or by injecting blood or sputum intraperitoneally into guinea pigs If P tularensis is present, these animals will die after a week or more and show typical areas of focal necrosis in the liver, spleen and lymph nodes in which clumps of P tularensis often can be found As the disease progresses, agglutinin for P tularensis usually appears in the blood, and the skin test made by injecting heat-killed bacteria intradermally becomes positive

In differential diagnosis, viral pneumonia, acute pulmonary tuberculosis, Klebsiella pneumonia, coccidioidal, histoplasmic, psittacotic and Q fever pneumonia must be considered

Prophylaxis

The *prophylaxis of tularemia itself* is outlined elsewhere in appropriate books There is no known method of preventing the development of *concomitant pneumonia* except by treating the disease itself Primary infection of the respiratory tract probably can be avoided by wearing an efficient mask when in contact with patients who have tularemic pneumonia or when working with infectious material

Treatment

Streptomycin is given intramuscularly in amounts of 1 gm every 12 hours Less may suffice, but larger amounts may be necessary in the severest cases Recovery usually occurs within 24 to 48 hours, but treatment should be kept up a day or two longer to forestall relapse

It is probable that tetracyclines[3] or chloramphenicol[4] will replace streptomycin for therapy Each can be given orally Tetracyclines are used in amounts of 1 5 gm every 6 hours for four doses, then 1 0 gm. to 1 5 gm every 6 hours for a total of 35 gm in about 7 days For severe cases, tetracyclines may be given intravenously in amounts of 500 mg every 6 or 12 hours for several doses before giving it orally Chloramphenicol is given initially in a 3 0 gm dose followed by 0 5 gm every 4 hours for 5 to 7 days

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PASTEURELLA PESTIS PNEUMONIA

(Pneumonic Plague)

Three clinical forms of plague are named bubonic septicemic and pneumonic The first two serve as sources of origin for pneumonic plague Depending upon the portal of entry —the skin in the bubonic form and the respiratory tract in the pneumonic form—the infection manifests itself clinically as two different diseases yet the causative microorganism is the same A similar diversity of clinical forms occurs in tularemia which is caused by a related bacillus

Etiology and Pathogenesis

Pasteurella pestis is a member of a group of bacteria which cause hemorrhagic septicemia For the most part the bacilli inhabit rodents as a commensal and from time to time circumstances permitting they are conveyed to man by various methods chiefly by infected rat fleas or by contact with infected blood or tissues The bubonic form almost always is accompanied by septicemia and bacilli are carried to the lungs by the blood Localization in the lung gives rise to specific plague pneumonia Primary pneumonic plague in other victims originates from this source by the inhalation of plague bacilli expelled and suspended in the air The bacilli settle on the mucous membranes of the respiratory tract or directly in the alveoli of the lungs and incite inflammation characterized by rapidly spreading hemorrhagic edema P pestis seems to be invasive without the aid of some other preceding condition to reduce the resistance but any preceding conditions no doubt favor their invasiveness Banal bacteria also may cause pneumonia in patients with plague

Epidemiology

Pneumonic plague may develop among persons suffering from bubonic plague but during an epidemic of pneumonic plague the bubonic form rarely occurs The source of pneumonic plague is a patient with plague pneumonia All susceptible persons near such a patient are in danger Pneumonic plague once it appears spreads from person to person rapidly in contrast with the bubonic form Crowding poor hygiene famine and other conditions less well understood favor the spread of infection In most instances severe epidemics occurred in the cold months Perhaps minor viral infections of the respiratory tract contribute to susceptibility and to the spread of pneumonic plague The disease is rare in tropical climates but it does occur there Pneumonic plague is believed generally to be highly contagious but recent observations have revealed numerous instances in which close contact did not result in disease[1,2] Plague bacilli occasionally are demonstrable for a short time in the throat of persons exposed to a patient These serve as carriers and may not become sick

The last great outbreak of pneumonic plague occurred in Manchuria in 1910–1911 during which 51 000 persons are said to have died in a 3 month period Plague is endemic in Asia Africa South America and islands adjacent thereto Small outbreaks of the pneumonic form occurred in California in 1919 in Rangoon in 1914 in Manchuria in 1946[3] and in Madagascar in 1952[4]

Pathology

The mucosa of the trachea and bronchi is inflamed and covered with a bloodstained frothy exudate Submucosal hemorrhages and necrotic patches may be present The pleural surfaces may be speckled with hemorrhagic areas Fibrinous pleural adhesions are found especially over the inflamed portions of the lung The lungs are congested and edematous Lobular foci are scattered throughout the lungs but often are adjacent to inflamed bronchi Confluence of a number of foci may cause a whole lobe to be affected The areas are dark grayish red but unlike those of pneumococcic lobar pneumonia contain no fibrin Microscopically edema and hemorrhage are prominent The bronchiolar walls in the inflamed areas are infiltrated with edema fluid leukocytes and erythrocytes The alveolar exudate is thin bloody and contains myriads of bacilli The lymphatics are engorged The tracheobronchial lymph nodes often are swollen soft and hyperemic with numerous ecchymoses There may be edema and hemorrhage of the anterior mediastinum

Symptoms

Pneumonia developing during the course of bubonic or septicemic plague is heralded by an increase of the gravity of the symptoms and signs referable to the lungs There is cough and thin often bloody sputum containing great numbers of plague bacilli

Primary plague pneumonia commences sometimes within a few hours usually 3 to 5 days after exposure to infection The onset is sudden often with a severe chill or chilly sensations There is a feeling of tightness and pain in the chest and dyspnea Cough is soft and easy There may be no cough or sputum for a day or so, but the signs of toxemia often are severe There is conjunctival injection flushing of the face headache anxiety, prostration and vomiting The temperature pulse rate and respiratory rate increase Drowsiness and delirium are common Later the face becomes dusky cyanotic and bloated

The sputum at first scanty becomes abundant thin mucoid frothy and bright red Frank hemoptysis occurs Plague bacilli are present almost in pure culture Patients later are too intensely ill or delirious to complain As the disease progresses the symptoms increase in severity until the patient gasps for breath cyanosis deepens ecchymoses appear generally and death results from toxemia, suffocation or failure of the circulatory system The temperature may drop to subnormal levels The disease seldom lasts longer than 4 days usually but 2

Abnormal physical signs in the chest often are surprisingly meager even in advanced cases There may be dullness on percussion in localized areas Rales strangely are occasionally absent until failure of the circulatory system and pulmonary edema develop Over pneumonic patches the breath sounds may be diminished or harsh Friction sounds are often present

Diagnosis

The recognition of cases in an epidemic is easy It is of greatest importance to detect and isolate strictly at the earliest possible moment the first case or cases of bubonic plague with concomitant pneumonia and also of course, patients with *primary pneumonic plague* to prevent spread of the infection The most certain method of diagnosis of pneumonic plague is the demonstration of plague bacilli in the sputum and blood stream by smear culture and by the inoculation of guinea pigs or rats Great care must be taken in handling infected materials Lung puncture or puncture of a bubo may be made to aspirate material for stained smear and for culture. The first few cases of the California epidemic were regarded as influenzal pneumonia until bipolar stained bacilli were found in smears made from the lungs at necropsy

Prognosis

The mortality rate generally is stated to be nearly 100% but numerous instances of recovery are on record some of which were achieved by modern therapy [1 3 4] Epidemics usually occur in primitive regions or in places ravaged by war or starvation Under these conditions it is highly probable that only the severe cases are diagnosed as pneumonic plague It is likely that mild and non fatal attacks occur and could be recognized if bacteriologic studies were made Not enough patients have been treated with new methods to estimate their effect on the death rate

Prophylaxis

Isolation is the most effective method to avoid pneumonic plague Patients with bubonic or pneumonic plague are not infectious until cough and sputum appear and may be transported with safety to hospitals for isolation According to standard recommendations attendants should be protected with complete sterile head masks with a celluloid window sterile gowns gloves and boots which must be worn whenever they are in the vicinity of patients and immediately sterilized after use These are uncomfortable and of doubtful value Prophylaxis by giving sulfadiazine in daily dosage of 3 to 6 gm to exposed persons for 1 week apparently was successful [1] Streptomycin or other antimicrobics also may be of prophylactic value Excreta sputum clothing bedding and utensils of patients must be sterilized The premises and bedding must be kept vermin free and rats must be de

stroyed. Vaccine and immune serum afford some degree of protection but it is safer to rely on other measures. Vaccination of living "attenuated" cultures of plague bacilli has been tested in Africa, with reported success. For details of methods the reader is referred to general articles on plague.

Treatment

To be successful treatment should be started within the first 24 hours of illness. Either tetracycline or chloramphenicol are given in doses of 500 mg. orally and 500 mg. intravenously. This dosage is repeated twice at 3 hour intervals, then 4 gm. are given orally per day for 2 days and 2 to 3 gm. a day for 4 or 5 days more. The average amount used by one group of observers was 22 gm. over 7 days.[4]

Streptomycin also is of value. It is given intramuscularly in 500 mg. doses every 3 hours for 2 days, then reduced to 1.5 to 3 gm. per day in divided doses over 6 or 7 days. If other bacteria are invasive, appropriate antimicrobics are applied. Cortisone given to several patients in addition to antimicrobics had no influence on the disease.[4]

Sulfadiazine or sulfamerazine may be used. Sodium sulfadiazine should be injected intravenously initially or continually depending on the condition of the patient and the response to therapy.

The symptomatic treatment is the same as for other pneumonias.

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ANTHRAX PNEUMONIA

The inhalation of dust from hides, hair, wool, grain or other substances contaminated with the spores of anthrax bacilli in rare instances may cause bronchitis and pneumonia. The onset usually is sudden with a chill or chilly sensation. Fever and other uncharacteristic symptoms and signs of pneumonia develop. Because of the unusual amount of edema incident to the infection there often are dyspnea, cyanosis and a sense of suffocation. The sputum varies in amount but may be thin, copious, bloody and foamy. The physical signs are those of patchy diffuse pneumonia and bronchitis with many moist rales. The signs change rapidly from place to place and in character. Areas of atelectasis occur. The mortality rate in untreated patients is high.

Pathologically there are patchy areas of hemorrhagic inflammation and thin exudate in the alveoli and bronchi. The regional lymph nodes usually are enlarged.

Diagnosis

The diagnosis is difficult unless a history of exposure to known sources of infection exists or if the bacilli are identified in the sputum, blood, pleural fluid or material obtained from the lung by aspiration with a hollow needle. Bacteriologic studies by cultural methods or by inoculation of guinea pigs are necessary.

Treatment

Because of the reported success of penicillin in the treatment of cutaneous anthrax, it should be used for pulmonary infection. It should be given in large doses, at first intravenously in amounts of 200,000 to 500,000 units, then intravenously or intramuscularly every 12 hours in similar amounts. The total dose may have to be increased to 4,000,000 units a day, depending on the therapeutic response.

Sulfadiazine is reported by some observers to be beneficial in cutaneous anthrax but penicillin is superior. No evidence supports the use of both agents in combination. Tetracycline also is said to be of value. The symptomatic treatment is the same as for other pneumonias. The source of infection should be found and proper control measures applied.

Symptoms

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GLANDERS PNEUMONIA

Pneumonias caused by Actinobacillus mallei and a related bacillus which causes melioidosis are rare. The disease usually is acute but may become chronic. There are no early characteristic symptoms or signs to distinguish it from other pneumonias. Diagnosis is aided by evidence of contact with a known or a probable source in animals, the later development of ulceration of the mucous membrane, a mucinous exudate and evidence of metastatic lesions elsewhere. Proof is obtained by isolating and identifying the causative agent by cultural methods or by inoculation of animals, and the presence of specific agglutinin in the blood. The disease usually is fatal and not enough observation has been made to judge the therapeutic value of antimicrobic therapy.

Streptomycin in doses of 1 to 3 gm. daily given intramuscularly is said to be effective.

CORYNEBACTERIUM DIPHTHERIAE PNEUMONIA

Pneumonia is one of the most frequent and dangerous complications of laryngeal diphtheria. It is present in most fatal cases. It usually is caused by the secondary invasion of a single species or a variety of bacteria commonly present in the oropharynx. In rare instances, the diphtheria bacillus is present alone but more often in company with other pyogenic bacteria. The sputum may contain many C. diphtheriae. The infection extends downward from the larynx to involve the trachea, bronchi and bronchioles causing formation of the typical membrane, and eventually involves the pulmonary tissue. C. diphtheriae may be found in the bronchial walls and in the bronchial and alveolar exudate.

The development of pneumonia during laryngeal diphtheria is indicated by an increase in fever, pulse and respiratory rate and cyanosis. The physical signs and roentgenographic shadows are those of a patchy peribronchial pneumonia. The treatment of the pneumonia depends on the causative agent. Diphtheria itself is appropriately managed with antitoxin, and if other bacteria are operative as well, the proper antimicrobic must be selected and used as indicated by tests of sensitivity.

Bacteroides Pneumonia

Bact. funduliformis, a commensal in the genitourinary and gastrointestinal tracts, in rare instances may cause pneumonia. The clinical course is uncharacteristic, but diagnosis may be made by isolating the bacillus from the blood, sputum, lung or pleural exudate. The pulmonary lesion consists of a diffuse infiltration of mononuclear cells, lymphocytes and erythrocytes. Multiple areas of necrosis are present in confluent patches of pneumonia. Chlortetracycline is said to be of value in therapy. In one group of 6 patients, 3 died.[1]

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PNEUMONIA IN TYPHOID

Pneumonia occurs as part of the clinical picture of many systemic infectious diseases. In some of them like the salmonelloses, shigellosis and in brucellosis, the lungs rarely, if ever, are the primary site of infection. As a rule, pulmonary involvement is blood borne and is one manifestation of systemic disease. It may be obscured by predominant signs and symptoms arising elsewhere. Pulmonary involvement was apparent in 64% of 80 patients with typhoid studied in Egypt, but pneumonia was diagnosed in only 11%. Studies failed to reveal Salmonella typhosa as a cause of the pneumonia. Pneumococci or other bacteria were thought to be responsible.[1]

In rare instances pneumonia may be caused by other *Salmonella*,[2,3] *colon bacilli*[4] and by S. typhosa in which the disease may begin suddenly, apparently as an infection of the respiratory tract with a sore throat and grippe-like symptoms. The fever is remittent or irregular. Tachycardia, dyspnea, cyanosis, pleuritis, empyema, bacteremia and arthralgia occur. The leukocyte count is variable. The pneumonic areas are patchy and scattered. Confluence of patches may give the signs of

consolidation The course lasts one to several weeks and fever declines by lysis

Since the pneumonia has no characteristic clinical features diagnosis can be made only by isolating and identifying the causative organism from the sputum pleural exudate or blood Specific agglutinin for the bacillus may appear and increase in titer after the first week To be of significance titers should exceed dilution of 1 100 and increase to higher levels in early convalescence

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A specific pneumonia may occur during the course of *granuloma inguinale*

PNEUMONIA IN BRUCELLOSIS

Pulmonary involvement in brucellosis rarely is noted but may be found occasionally if sought for The pneumonia is hematogenous in origin and usually is obscured by other symptoms of the disease References to pertinent literature are gathered in Harvey s paper[6]

About one third of patients with brucellosis have cough and some of them raise purulent sputum Pneumonia is present in only a few as an episode in the usual course of the disease It is low grade transitory or chronic and unless the underlying disease is recognized it may be confused with pulmonary tuberculosis Q fever histoplasmosis or coccidioidomycosis

The signs symptoms and roentgenographic changes of pneumonia caused by or presumably caused by brucellae are uncharacteristic and etiologic diagnosis is impossible unless the primary disease is recognized and brucellae are found in the sputum or pleural exudate if any The pulmonary infiltrate lasts variable lengths of time usually several weeks or months and may become chronic Pneumonia in brucellosis may be caused by unrelated microbes

In several cases of chronic brucellosis pulmonary disease identified with Loeffler s syndrome was observed[7] An allergic aspect probably was involved In rare instances granulomatous nodules may persist They may be mistaken for tuberculomas neoplasms and other lesions[8]

Treatment

Treatment is the same as for systemic brucellosis Some physicians recommend a combination of chlortetracycline in doses of 750 mg every 6 hours with 1 gm of streptomycin injected intramuscularly twice daily for 12 or 14 days If prolonged therapy is needed the amount of streptomycin is reduced to 0 5 gm doses Others add sulfadiazine to the combination Still others report success with the use of chloramphenicol or tetracycline The therapeutic problem is unsettled

Adrenocorticotropic hormones may be helpful in severe cases if an allergic factor is operative

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PSITTACOTIC-ORNITHOTIC PNEUMONIA

Psittacosis and ornithosis are related diseases of psittacine (parrot family) birds marine birds barnyard fowl and others[1] Man is infected by contact with sick or with healthy

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PNEUMONIA IN BRUCELLOSIS

Pulmonary involvement in brucellosis rarely is noted but may be found occasionally if sought for. The pneumonia is hematogenous in origin and usually is obscured by other symptoms of the disease. References to pertinent literature are gathered in Harvey's paper.[6]

About one third of patients with brucellosis have cough and some of them raise purulent sputum. Pneumonia is present in only a few as an episode in the usual course of the disease. It is low grade, transitory or chronic, and unless the underlying disease is recognized it may be confused with pulmonary tuberculosis, Q fever, histoplasmosis or coccidioidomycosis.

The signs, symptoms and roentgenographic changes of pneumonia caused by, or presumably caused by, brucella are uncharacteristic and etiologic diagnosis is impossible unless the primary disease is recognized and brucellae are found in the sputum or pleural exudate, if any. The pulmonary infiltrate lasts variable lengths of time, usually several weeks or months, and may become chronic. Pneumonia in brucellosis may be caused by unrelated microbes.

In several cases of chronic brucellosis pulmonary disease identical with Loeffler's syndrome was observed. An allergic aspect probably was involved. In rare instances granulomatous nodules may persist. They may be mistaken for tuberculomas, neoplasms and other lesions.[8]

Treatment

Treatment is the same as for systemic brucellosis. Some physicians recommend a combination of chlortetracycline in doses of 750 mg. every 6 hours with 1 gm. of streptomycin injected intramuscularly twice daily for 12 or 14 days. If prolonged therapy is needed the amount of streptomycin is reduced to 0.5 gm. doses. Others add sulfadiazine to the combination. Still others report success with the use of chloramphenicol or tetracycline. The therapeutic problem is unsettled.

Adrenocorticotropic hormones may be helpful in severe cases if an allergic factor is operative.

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PSITTACOTIC-ORNITHOTIC PNEUMONIA

Psittacosis and ornithosis are related diseases of psittacine (parrot family) birds, marine birds, barnyard fowl and others.[1] Man is infected by contact with sick or with healthy

birds that carry the organisms or by exposure to dust of their feces feathers and skins[6] Person to person infection has been reported Cases are often sporadic but localized outbreaks occur among persons exposed to single or multiple sources of infection as in poultry handlers pet fanciers and laboratory workers The pathogens are microbes of the Miyagawanella group They are filtrable coccoid bodies smaller than rickettsias larger than true viruses and are susceptible to the effect of antimicrobic agents

Pathology

The mucous membrane of the upper respiratory tract may serve as a portal of entry of the virus but rarely is affected The chief lesions of the disease occur in the lungs In most cases the gross findings are those of patchy areas of focal or lobular infiltration that start near the hilum and spread outward in a sequence of congestion edema red and subsequently grey hepatization or splenization All stages may be present at once Occasionally several lobes may be affected The pleura seldom is involved On section the areas are grayish red moist somewhat gelatinous and mottled more uniform than in the usual form of lobular pneumonia but less dense than in lobar pneumonia Bronchitis is not an important feature

Microscopically the lesion is similar to that caused by viruses In the earliest stages no bacteria are present but minute coccoid bodies may be found in large phagocytic cells and in mononuclear cells present in the alveolar walls The alveolar walls often are necrotic or hemorrhagic There is cellular invasion of the interstitial tissue hyperplasia and desquamation of the alveolar epithelium and exudation of mononuclear cells fluid and fibrin into the spaces There is often an infiltration of lymphocytes and plasma cells into the bronchial walls and the lumens contain a serous exudate rich in mononuclear cells The regional lymph nodes are hyperplastic In later stages lesions caused by other bacteria may be present

Symptoms

After an incubation period of about 10 days the disease begins abruptly with malaise anorexia chills headache fever photophobia and sweating A typhoid like state may confuse the diagnosis The fever is remittent or continuous often at high levels and in favorable cases without treatment falls by lysis in a week or more The pulse rate and respiratory rate usually are slow in proportion to fever except in severe cases All grades of severity of disease occur from inapparent or symptomless infection especially in ornithosis to fulminating fatal disease[3]

The severity of the disease is not always in proportion to the extent of the pneumonia The signs usually are those of uncharacteristic pneumonia The signs and symptoms may closely resemble those of pneumococcic lobar pneumonia except that headache abdominal distention and profuse sweating are more prominent and pleural pain is uncommon There may be no sputum or sputum of a tenacious quality rusty or blood streaked may be raised Ulcerative stomatitis occurs The upper respiratory tract rarely is involved

Abnormal physical signs in the lung may not be found for a day or two but shadows often can be demonstrated by roentgenography during the first 48 hours Later there are rales in scattered areas which shift from place to place as the inflammation migrates When large areas are involved there may be dullness with decreased tactile fremitus diminished or increased intensity of breath and voice sounds and numerous rales Signs of consolidation may be audible over massively involved lobes

The roentgenographic shadows resemble those of viral pneumonia The lower lobes often are first affected Early in the disease there is a faint shadow near the hilum which spreads outward for several days until a whole lobe may be obscured by a diffuse homogeneous density unlike the mottling usually found in the other forms of pneumonia and not so dense as in pneumococcic lobar pneumonia The lesion often spreads gradually while clearing occurs in areas first affected Involvement of the other lung may begin while lesions in the lung first attacked disappear

Laboratory Data

The leukocytes may be decreased normal

or slightly increased in number. The germs are found regularly in the sputum and but seldom in the blood. Complement-fixing antibodies develop during early convalescence and rise in titer.

Diagnosis

Clinical diagnosis may be made in patients with pneumonia if the pulse rate and respiratory rate are slow, if grip-like or typhoid-like symptoms are present and the leukocyte count is low, and if there is a history of intimate contact with sick or well birds or with patients ill with the disease. The aid of roentgenography in diagnosis was mentioned. Positive diagnosis can be made by injecting sputum or material obtained from the lung by aspiration with a needle intraperitoneally into mice; the animals usually die after 10 days to 2 weeks. If pneumococci or other bacteria pathogenic for mice are present, the sputum must be filtered before inoculation. Necropsy reveals focal necrosis of the liver and spleen, and Miyagawanellae are present in mononuclear cells. Care must be used to prevent infection of laboratory workers. The complement-fixation test, if a rising titer occurs during convalescence, is of value in diagnosis but does not differentiate psittacosis from ornithosis. In differential diagnosis viral pneumonias, typhoid pneumonia, Q fever, histoplasmosis, coccidioidomycosis and tularemic pneumonia must be considered.

Prognosis

The duration of moderately severe disease in favorable cases without antimicrobic treatment is one or three weeks. Bad prognostic signs are the evidence of massive involvement of the lung, circulatory failure and, of course, the presence of other chronic illness, or the development of complications caused by bacteria. The mortality rate in untreated patients is probably lower than the usually stated 35 or 40%. Many mild cases are undiagnosed. The prognosis is better in young persons. Treatment with antimicrobics improves the prognosis.

Prophylaxis

Avoidance of contact with birds of the varieties known to harbor the disease is the most reliable prophylactic measure. Those obliged to handle birds or feathers or those engaged in investigating the disease are liable to infection. The wearing of rubber gloves, gowns and masks, eye shields and impervious hoods minimize the danger of infection. Prophylactic vaccines may be perfected eventually. Sputum from patients is infectious and must be treated with germicides or burned.

Sick birds of any species should be killed and buried or burned. Birds which have been in contact with sick ones should be quarantined for several weeks. Even with these precautions the possible presence of carriers among healthy birds is an ever present danger.

Treatment

Tetracycline, chlortetracycline or oxytetracycline are the drugs of choice. The dose is 1 to 2 gm. orally every 6 to 8 hours for the first 2 days and every 12 hours for a week. Penicillin is effective in amounts of 200 000 to 400 000 units (120 to 240 mg.) daily given intramuscularly. The symptomatic treatment is the same as for viral pneumonia (page 133).

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RICKETTSIAL PNEUMONIAS

Typhus, Rocky Mountain spotted fever and scrub typhus (tsutsugamushi disease) are systemic diseases caused by Rickettsia during which the lungs may be involved. It usually is difficult to decide whether the pneumonia is specific or caused by superinfection with bac

teria or by bacteria alone The pneumonia has no distinguishing features unless pneumococci hemolytic streptococci or staphylococci are operative and the clinical course assumes characteristics of the respective infection For purposes of specific antimicrobic therapy it is important to determine the cause

In *epidemic typhus* pneumonia may occur in 30% of patients and is one of the chief causes of death It occurs less often in *endemic (murine) typhus* and in *Rocky Mountain spotted fever* Among the Armed Forces of World War II in the South Pacific region *scrub typhus* was common and two thirds of the victims had pulmonary involvement which resembled viral pneumonia Only one died

TREATMENT

The treatment of pneumonia in each of the rickettsial diseases is the same For the specific lesion chloramphenicol or a tetracycline drug is given orally in initial dosage of 2 to 4 gm followed by 2 to 4 gm daily in 3 or 4 divided doses The drugs may be injected intravenously if oral administration is not possible In severely sick patients cortisone may be given in addition It is given orally or injected intramuscularly in amounts of 200 mg the first day 100 mg the second 50 the third If other bacteria are operative the major pathogen should be identified and appropriate antimicrobic therapy applied Symptomatic treatment of the pneumonia is the same as for viral pneumonia (page 133)

Q FEVER PNEUMONIA

Q (Query) fever is caused by rickettsia like agents called Coxiella burneti It is found world wide Cattle sheep and goats and their hair hides meat milk and dust from their manure are the chief sources of infection[8] Infection usually is airborne but may occur by ingestion of infected milk and otherwise Milk was thought to be a source for a large number of persons in California whose blood contained immune bodies indicative of previous unrecognized infection The disease is a systemic one and in its severe forms a viral like pneumonia is its chief feature The upper respiratory tract rarely is involved Pulmonary lesions in the few cases studied at necropsy resembled those of viral pneumonia (Fig 12) Coxiella may be seen intracellularly

Clinical

Most victims have uncharacteristic mild disease usually mistaken for grip The incubation period is 16 to 21 days In more severe attacks with pneumonia the onset often is abrupt with fever headache weakness and a chill or chilliness Later there are an unproductive cough chills drenching sweats pain in the chest photophobia pain in the eyes and relative bradycardia In some instances meningoencephalitic symptoms are dominant In some severe cases the lungs are not involved in others the degree of sickness is not in proportion to extensive pulmonary involvement The cough may be paroxysmal and the scanty sputum raised may be streaked with blood The respiratory rate seldom is increased but slight cyanosis may be evident The case of moderate severity lasts 1 to 2 weeks Fever declines by lysis and convalescence is uneventful Relapse may occur Chronic disease lasting five months has been observed

Of importance as in viral pneumonia is the disproportion between the extent of pneumonic roentgenographic shadows and the paucity of physical signs Occasionally there is dullness but rarely signs of consolidation The lesions are patchy and in both lungs Phlebothrombosis pleurisy pleural effusion arthralgia orchitis epididymitis esophagitis intestinal hemorrhage and decubitus ulcers may occur during the disease or as sequels

There are no important changes in the blood count or urinalysis The sedimentation rate of erythrocytes may be increased slightly

Diagnosis

Unless the disease is in mind or sought for it is easily confused with what is called grip and with viral pneumonia histoplasmosis coccidioidomycosis psittacosis or other diseases If symptomless Q fever pneumonia may be undetectable unless abnormal pulmonary shadows are seen in roentgenograms or serol

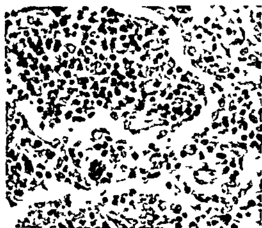


Fig 12 Q fever pneumonia Swollen alveolar epithelium and monocytes fibroblasts and lymphocytes compose the exudative and infiltrative reaction (Courtesy of Dr R D Lillie) (From Reimann *Pneumonia* Springfield Thomas 1954)

ogic tests are made The occupational or environmental history is helpful

Diagnosis is established in specially equipped laboratories by the isolation of Coxiella from the sputum blood urine or pleural exudate Manipulation of infected material is dangerous A rise in the titer of complement fixing antibodies in the serum beginning in the convalescent phase is an important aid An unchanging low titer of 1 32 or less is of no significance Cold agglutination of erythrocytes does not occur

Prevention

Avoidance of contact with infected animals or their products is of greatest importance A vaccine is available for persons necessarily subjected to exposure but its value is undetermined Pasteurization of milk does not always render it safe but boiling is effective In several instances recognition of the disease in a patient led to epidemiologic studies and the discovery of numerous other instances of Q fever current or past in groups of persons exposed to the same sources of infection

Treatment

The symptomatic treatment is the same as for other forms of pneumonia Tetracycline drugs and chloramphenicol both have been reported to cause clinical improvement Experiments in cattle however show that chlortetracycline does not eliminate Coxiella from the milk No antimicrobic therapy is needed in mild cases If necessary one of the antimicrobics named is given orally in an initial dose of 2 or 3 gm for an adult, and 2 gm daily thereafter in divided doses until the temperature is normal for several days Occasionally neither is helpful [3]

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MYCOTIC PNEUMONIAS (See Chapter 9)

ARTHROPOD PNEUMONIA ACARIASIS OR ACARINOSIS

The arthropod Tyroglyphus tarsonemus was found in the sputum of patients with recurrent bronchitis or mild pneumonia in the East and West Indies and in India The disease resembles the Loeffler syndrome and apparently is caused by the mite The mites probably are inhaled with the dust from vegetation on which they reside

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RHEUMATIC PNEUMONIA

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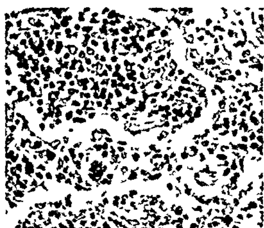


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RHEUMATIC PNEUMONIA

Pneumonia occasionally occurs during the course of acute rheumatic fever but it often

is impossible to decide whether it is caused incidentally by unrelated bacteria or viruses[1] or if it is a specific lesion of rheumatic disease itself. Many observers believe that most of the manifestations of rheumatic fever including rheumatic pneumonia are the results of a hyperergic reaction to a recent infection with group A hemolytic streptococci.[2] The lungs apparently are affected specifically in about 1% of patients with severe rheumatic fever. The pneumonia seldom is recognized clinically but it is found at necropsy in about 50% of patients who die from rheumatic fever. The acute pulmonary lesions in most instances are transitory. They may lead at times to permanent fibrotic or other changes which eventually cause cardiorespiratory embarrassment.

Pathologically both lungs usually are involved with lesions varying in size from small hemorrhagic foci to rubbery consolidation of a lobe. Atelectatic areas often are present. Microscopically lesions of rheumatic fever are present in the pulmonary arterial system, perivascular areas and the pulmonary interstitial tissue. Rheumatic granulomas are present, sometimes as Aschoff nodules or in large aggregations of densely packed endothelial cells, leukocytes and detritus. The alveolar walls and elastic tissue may be destroyed. Congested and hemorrhagic areas and exudate composed of serum, fibrin, leukocytes and red cells are present. A number of observers believe the lesion to be characteristic of rheumatic infections but not specifically so. The changes often resemble those present in viral pneumonia, polyarteritis, uremia and after chemical irritation.[3,4] Interstitial fibrosis may result as a sequel.

Symptoms

The specific pneumonia of early rheumatic fever may be confused with atelectasis, with pulmonary congestion from toxemia or heart failure, or in later stages of the disease with secondary bacterial pneumonia. The symptoms of specific pneumonia usually develop in patients during a severe attack of rheumatic fever and may appear with evidence of carditis. The pulmonary signs and symptoms may be overshadowed by others elsewhere but may dominate the picture especially in children. The symptoms of rheumatic fever such as fever, sweating and arthritis usually are present. The pneumonia being part of the disease or an episode in it is not preceded by infection of the upper respiratory tract as the common forms of pneumonia so often are nor does it begin abruptly with a chill. There may or may not be an increase in the severity of symptoms when pneumonia begins. Slight cough occurs with a small amount of tenacious occasionally blood streaked sputum remarkably free from bacteria. Pain in the chest is not common unless pleuritis is present. The fever may be irregular and high, and tachycardia and tachypnea are present. The number of leukocytes and the sedimentation rate of erythrocytes are increased.

The physical signs or roentgenographic evidence suggest pulmonary involvement. Small patchy areas of congestion may be found which change in location from day to day, or a whole lobe or several lobes may be consolidated. Dullness, bronchial breathing, weak bronchophony and a few rales may be heard. The signs of consolidation usually persist for 3 or 4 days in one place or may last more than a week. Evidence of consolidation may recur in an area previously affected. Signs of atelectasis or pleural effusion commonly are present and friction sounds often are heard. Roentgenograms may be disappointing and indefinite but often show patches of density usually near the hilums of both lungs, changing in location from day to day, and an increase in the bronchovascular marking. Occasionally whole lobes are dense.

The prognosis of patients with rheumatic pneumonia is of course serious because the pneumonia usually occurs in severe cases.

Diagnosis

Symptoms or signs of pulmonary involvement present during severe rheumatic fever without previous infection of the upper respiratory tract should suggest specific rheumatic pneumonia. The disproportionate mildness of symptoms referable to the lung in contrast with the extent of the lesion found by physical examination or by the roentgenogram is characteristic. Prompt improvement follow

ing anti rheumatic treatment favors a diagnosis of specific pneumonia. The specificity of the lesion can be proved postmortem by histologic examination. Pneumonia caused by the ordinary bacteria must be ruled out by appropriate bacteriologic or serologic tests.

Treatment

Except for routine symptomatic care as for other forms of pneumonia the treatment is the same as for rheumatic fever. Anti rheumatic drugs such as aminopyrine and sodium salicylate often relieve the discomfort. Rheumatic pneumonia no doubt will respond to therapy with cortisone and adrenocorticotrophic hormone as other rheumatic manifestations do. If pneumonia is caused by bacteria appropriate antimicrobic therapy is indicated.

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TREPONEMA PALLIDUM PNEUMONIA, SYPHILITIC PNEUMONIA

Pneumonia caused by Tr pallidum is a rare disease, and no doubt is becoming rarer as syphilis itself is controlled by modern management. Syphilis affects the lung in two general forms one as an acute interstitial pneumonia and the other by the formation of gummas. In the so-called "white lung" of new born syphilitic infants the lungs are pale and firm or blotched with light colored areas caused by hyperplasia of fibrous tissue in the interstitial areas. The alveoli are filled with epithelial cells fat and macrophages containing Tr pallidum.

There is controversy as to whether a specific form of syphilitic pneumonia occurs in adults but it does. It occurs more often than is believed and could be found if sought. As in other systemic diseases specific pneumonia often cannot be differentiated clinically from intercurrent disease caused by secondarily invading microbes.

In untreated patients pulmonary syphilis is said to occur in 1 out of 20 cases of visceral syphilis chiefly in males in the third decade of life. In published reports of cases the lesions were confined to one lung but both lungs may be involved. Any portion of the lung may be affected and when lesions occur in the upper lobes they may be mistaken for tuberculosis. Syphilitic pneumonia may occur a number of weeks to years after the initial infection. It may occur as an episode in the earliest stages of syphilis during the period when the mucous membrane of the respiratory tract is involved. It is believed that pneumonia may be caused at times by an extension of treponemal infection of the bronchi into the bronchioles and alveoli but more likely as a result of the development of specific syphilitic granulomas in the perivascular tissues of the lung. In certain cases multiple infarcts of different ages are found scattered in both lungs with numerous thrombotic blood vessels. They no doubt are the result of local specific vascular disease. After a variable period the lesions in the lung tend to resolve spontaneously but they may recur persist and end in a chronic process with fibrosis or caseation.

Pathology

In syphilitic pneumonia the foci are demarcated and firm especially in the advanced stages. They are gray with yellowish patches. The lesions often are clustered around the hilum adjacent to the larger blood vessels.

Microscopically the lesion begins as an accumulation of cells and growth of connective tissue adjacent to blood vessels. Granulomas form in the alveolar walls and miliary syphilomas develop in the alveoli. The interstitial tissue is infiltrated with cells which often results in the collapse of the adjacent alveoli. Other alveoli may be dilated or contain lymphocytes. In places epithelioid cells are found with multinucleated giant cells resembling

tubercles The small bronchi and adventitia of the blood vessels are thickened by infiltration with lymphocytes and plasma cells Periarteritis and less often endarteritis are found The changes according to roentgenographic evidence may regress and disappear after specific therapy but may progress and become *chronic with fibrosis* or atrophy

Symptoms

The pneumonia may occur weeks months or years after the initial infection The onset is insidious and there is seldom any fever or sweating The symptoms are usually those of a low grade pneumonia and lead one to suspect pulmonary tuberculosis Pain in the chest may be noted and cough with mucopurulent sputum occurs in nearly all cases Dyspnea and hemoptysis occur in about one half of the patients

The physical signs vary greatly in degree and extent Rales are the most constant finding In a few patients no changes in percussion or auscultatory sounds are present in the majority the signs are those of patches of consolidation especially near the hilums or involving a whole lobe Roentgenograms show lesions otherwise not detectable during life The shadows are not specific for syphilis however and are similar to those of the more common forms of patchy pneumonia with the densest lesions near the hilum especially in the lower or middle lobes a point of contrast with tuberculosis

Diagnosis

The development of symptoms of mild but persistent pneumonia in a patient with syphilis should lead one to suspect invasion of the lung If systemic syphilis is not suspected it is of course almost impossible to arrive at a correct diagnosis In patients with an indolent form of pneumonia and if no significant bacteria can be found in the sputum syphilis should be thought of It is highly important in every case not to focus the attention on the lungs alone but to consider the patient as a whole A history of infection other signs of syphilis and positive serologic tests are of importance Diagnosis of pulmonary syphilis is aided if T pallidum can be demonstrated in the sputum but care must be taken not to confuse that organism with the usual spiral microorganisms found normally in the mouth Rabbits may be inoculated intratesticularly with sputum and if T pallidum is present typical syphilitic lesions will appear If the pulmonary lesions disappear promptly after treatment with penicillin it is probable though not certain that they were syphilitic in nature Pneumonia caused by bacteria must be considered Positive diagnosis can be made only by histologic examination of the lung In differential diagnosis other low grade infections must be ruled out such as those caused by fungi tuberculosis and bronchiectasis

Treatment

The treatment is the same as that for the usual forms of syphilis

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FUSOSPIROCHETAL PNEUMONIA

It is doubtful that bacteria of fusiform or spiral shape so commonly found in the oropharynx are the cause of pneumonia They almost always are present in and around the gingival margins and can be found in the scrapings of mucous membrane in saliva and in the cheesy substance normally present in the tonsils They are present in the pus of bronchiectatic cavities lung abscess and other pulmonary disease

Since these bacteria are saprophytic they multiply greatly when necrotic tissue is present and myriads of them in pus sputum and in diseased areas do not necessarily indicate their pathogenicity

From time to time reports of cases of fusospirochetal pneumonia appear but in none is there sound evidence of a causal relationship of the bacteria to the disease It is probable that the pneumonias in most cases were caused

by some primary invader or some other disease was present which provided necrotic material favorable for the multiplication of the so called fusiforms and spirals

In the face of this uncertainty it is illogical to use spirocheticidal drugs in the treatment of patients whose pulmonary exudate contains fusiforms and spirals Fusospirochetal organisms swarmed in the secretions of patients who at one time were under intensive treatment with arsphenamine for syphilis Furthermore there is no reason to believe that modern therapy so effective in the treatment of infection due to Tr pallidum will also injure other forms of microorganisms simply because they have a spiral shape An underlying condition should be sought instead and treated appropriately with antimicrobics or other indicated measures

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PNEUMONIAS IN PROTOZOAL INFECTIONS

PNEUMONIA IN MALARIA

Pneumonia occasionally occurs during malaria It still is uncertain whether it is caused specifically by the plasmodia and if so in what percentage of cases Pneumonia may result from secondary bacterial invasion of pulmonary tissue if its resistance is diminished by malaria or if atelectasis occurs Small hemorrhages incident to the blocking of small pulmonary blood vessels by deposition of erythrocytes plasmodia and pigment also may play a role in favoring secondary infection In a few instances plasmodia were demonstrated in sputum in tissue obtained by lung puncture and in hemorrhagic pleural effusion Recovery occurred after specific therapy was used The pneumonia may be recurrent Literature on the subject is reviewed elsewhere [1]

In one series of cases pneumonia occurred in about 4% of patients with malaria mostly in the *season when both malaria and pneumonia* were most prevalent [2] It was not possible to decide whether pulmonary lesions were caused by the plasmodia or by coincidental viral or bacterial infections A similar observation was made in India [3] The signs and symptoms of pneumonia were uncharacteristic and resembled those of viral pneumonia clinically and roentgenographically Monocytosis and splenomegaly were suggestive diagnostic points The average time spent in the hospital was 17 days An unstated percentage of patients was aided by antimalarial therapy some by sulfonamide compounds and in others neither form of treatment was effective But British clinicians regard the relation of pneumonia to malaria as fortuitous

AMEBIC LESIONS OF THE LUNG

The lungs are the third most common site of localization of the Endamoeba histolytica Pulmonary involvement is chiefly the result of the rupture of an amebic abscess of the liver through the diaphragm but under such circumstances the lesion may be regarded as an abscess and not pneumonia [4] In protracted cases of amebic dysentery the reduction of resistance incident to chronic debilitating disease may lead to pneumonia caused by bacterial infection [5] In rare instances the amebas may be carried to the lung by the blood stream and cause pneumonia Abscesses may form later in the involved areas The abscesses contain a mucinous substance with red cells large mononuclear cells debris and amebas Around the abscesses the alveolar walls are thickened by an acute inflammatory reaction and the air sacs contain fibrin and debris but few leukocytes Amebas often are distributed irregularly in the interstitial tissue and alveolar spaces According to Hoff and Hicks an allergic manifestation in the lung and eosinophilia characteristic of Loeffler s syndrome or transient eosinophilic pulmonary infiltration occur during intestinal amebiasis [6]

There is nothing characteristic from a clinical point of view about the pneumonia associated with amebas in patients with amebic dysentery It is difficult to differentiate it from the

common forms of pneumonia of mixed bacterial origin which accompany or follow any chronic debilitating diseases. Amebas may be found in the sputum, and evidence of abscess formation ultimately appears. Pleuritis may occur. Recovery should occur promptly if an amebacidal drug is given early before extensive necrosis occurs.

In one series of 170 cases of amebiasis, roentgenographic evidence of thoracic involvement was present in 16.[7] In 6 there was patchy infiltration of the right lower lung field, in 2 there was an abscess and in 7, pleural effusion. Nine patients had pain in the area. An enlarged liver may raise the right leaf of the diaphragm and obliterate the costophrenic angle. Abnormal shadows in the adjacent lobe of the lung may be due to atelectasis, to amebic pneumonia or to an abscess. Evidence of disease in the right lower lobe should suggest amebiasis in regions where the disease is endemic.

The specific treatment is the same as that used in amebic dysentery, as described in appropriate books on the subject. Emetine hydrochloride is the drug of choice. Chloroquine and certain antimicrobic agents which act favorably in the treatment of amebic abscess of the liver and intestinal amebiasis, disappointingly, have no significant effect on the specific pulmonary lesions. If secondary bacterial infection occurs, the appropriate antimicrobic should be selected for therapy.

PNEUMONIA IN KALA AZAR

Pneumonia is a frequent cause of death in untreated patients with kala azar. Most often it is caused by invasion of the lungs by the usual variety of bacteria which inhabit the nasopharynx. Invasion is made possible by the diminished resistance of a patient incident to the severe systemic disease or to actual specific damage of pulmonary tissue caused by Leishmania donovani. Since these hemoflagellates invade lymphoid and endothelial tissue generally, but especially the spleen, liver and bone marrow, there is reason to believe that the lymphoid and endothelial tissues of the lung may be invaded similarly. If carefully sought, specific lesions may be found in the lung in the form of groups of endothelial cells in obstructed capillaries, some of them degenerated and vacuolated and some containing the microorganisms. Parasite laden endothelial cells may be found in the alveolar walls. Other unplugged capillaries may be congested. In the cases studied, clasmatocytes were found in the alveolar spaces, but no Leishman-Donovan bodies were seen in them. There may be hemorrhage into the alveoli and scattered patches of pneumonia and atelectasis.

TOXOPLASMIC PNEUMONIA

Toxoplasmosis is a disease caused by a protozoan which resides intracellularly in mononuclear and epitheloid cells, endothelial cells of capillaries, in leukocytes, nerve cells and others. Descriptions of the systemic disease are given elsewhere.[8] Toxoplasmosis is found chiefly in infants, but cases in adults occur. In older children and adults it is characterized chiefly as a severe systemic disease with an exanthem and pneumonia.[9] The pneumonia resembles viral pneumonia clinically and pathologically except that toxoplasma can be demonstrated in the lesions and in the exudate (Fig 13).

PNEUMOCYSTIS PNEUMONIA

Pneumonia suspected to be caused by a doubtful protozoan Pneumocystis carinii has [illegible] in America as cytomegalic plasmacytic inclusion pneumonia, to be caused by the same parasite[10] (see page 136, Viral Pneumonia). The disease affects debilitated persons chiefly, and the mortality rate is 30 to 40%. The parasite can be visualized microscopically in pneumonic areas. The hosts of the parasite are domestic animals and rodents.[11]

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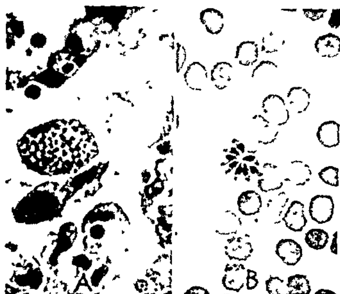


Fig 13 Toxoplasmic pneumonia A An infected cell filled with toxoplasma bodies lies free in an alveolar sac B Appearance of toxoplasma in a stained smear preparation (Courtesy of Dr Henry Pinkerton) (From Reimann *Pneumonia* Springfield Thomas 1954)

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PNEUMONIA IN METAZOAL DISEASES

Pneumonia occurs in metazoal diseases as the helminths migrate through the lungs during a phase in their life-cycles When only a few pass through after a light inoculum no detectable pulmonary changes occur when there are many pneumonia becomes evident clinically Pneumonia also may be caused by bacteria or viruses as a coincidental infection An allergic response of the lung called Loeffler's syndrome may occur and presumably is caused by the reaction of sensitized pulmonary tissue to circulating specific antigen from sources elsewhere in the body

Specific pneumonia appears only in *ankylostomiasis ascariasis* and *strongyloidiasis* when as part of their life cycles larvas escape through the blood vessels into the pulmonary parenchyma during their transient passage through the lungs In *filariasis, trichiniasis* and *schistosomiasis* larvas pass through the lungs without escaping from the vessels but their presence may incite a reaction probably allergic and cause pneumonia In schistosomiasis metacercariae may escape from the blood vessels into the pulmonary tissue In *paragonimiasis* metacercariae pass from the

abdominal cavity through the diaphragm and pleura penetrate the lung and lodge in bronchioles They cause pneumonia and later abscesses cysts fibrosis and chronic disease resembling tuberculosis Tuberculosis often is coexistent In *echinococcosis* organisms at *times lodge in the lungs* The cysts which form act as foreign bodies and as such may cause pulmonary inflammation often called peripneumonia

The degree of severity of the pulmonary reaction depends largely on the size of the original inoculum of the microorganisms *mentioned* *The gravity of the disease* also depends on the age and the physical state of the patient Pneumonia appears from several days to a week after infection according to the life cycle of the causative metazoan It may be mild and undetectable except by roentgenography or severe and even fatal The course lasts several days to a week or more Bronchiolitis and bronchitis occur The pulmonary lesion is patchy hemorrhagic and contains leukocytes often with eosinophile cells predominant Secondary bacterial in*vasion may occur*

An *eosinophilic systemic and pulmonary reaction* called Loeffler s syndrome may appear and recur in each of the metazoal diseases mentioned These allergic manifestations occur after *reinfection or in chronic cases* as a result of previous specific sensitization

Diagnosis

Early diagnosis may be impossible since pneumonia often is the first evidence of infection with metazoa Later in the course when other characteristics appear the correct diagnosis may be suspected and proved by demonstrating the causative larvas or eggs in the sputum and elsewhere according to the disease at hand Even then it is not possible without necropsy to determine the degree of participation if any of secondarily invading bacteria They may be the sole cause even if larvas or eggs are in the sputum

Treatment

There is no specific treatment for the pneumonia in the early stages of the respective diseases Later when the diagnosis is made therapy is applied as described for the disease itself An allergic reaction may be *controlled* with pituitary adrenocorticotropic hormones but no report of their use in these diseases have come to my attention

PNEUMONIAS CAUSED BY MIXED INFECTION SECONDARY TO *ACUTE AND CHRONIC DISEASES, SHOCK, SENILITY, MECHANICAL* CAUSES, ETC

In the preceding sections the acute pulmonary diseases caused by a single infectious agent were discussed It is probable however that the majority of acute bacterial inflammations of the lungs are of indeterminate mixed bacterial origin Many pneumonias of this kind are unsuspected during life or are obscured by some condition which predisposes *patients to them* The pneumonias often are unrecognized ignored and not recorded in clinical or in statistical reports They often are discovered at necropsy

CAUSATIVE FACTORS

The upper air passages normally harbor a variety *of potentially* pathogenic microbes The descending air passages contain *fewer and fewer until none are found in the* peripheral portion of the lung Ciliary activity a slight peristaltic motion of the air *tubes and* cough serve as a complex mechanism *which* tends continuously to eject *foreign particles* caught in the normal *mucoid secretion* If a few microbes pass this barrier and enter the alveoli they are disposed of by *phagocytic* cells or enzymes carried off *by the lymphatics* or simply die for want of *favorable conditions for growth* If at any time this delicate equilibrium is disturbed conditions may permit the entrance growth and invasion of bacteria and the development of inflammation *that is* pneumonia For unknown *reasons* either a *single variety of* bacteria may cause pneu

monia as described in preceding sections or as discussed here two, three or more kinds of bacteria seem to participate. Only a few of the many varieties of bacteria present succeed in causing disease. Pneumococci are the chief pathogens, but hemolytic streptococci, staphylococci, Klebsiella, H. influenzae, G. tetragena and others participate.

PREDISPOSING FACTORS

Many factors predispose to pneumonia, among which the following are of importance:

Infectious Diseases

In most of the pneumonias caused by viruses, secondary bacterial infection may occur, especially in severe cases and late in the disease.

Other Diseases and Conditions

Chronic debilitating disease of any sort, such as cardiac failure, nephritis, arteriosclerosis, diabetes, hepatic cirrhosis, anemia, malnutrition, the feebleness of early infancy and of old age, and many other conditions all are predisposing factors. Diseases of the lung like asthma, bronchiectasis, abscess, foreign body, tumors, cysts, aneurysms, amyloid and lipoid deposits, emphysema, infarcts, atelectasis and others often are characterized by single or repeated pneumonic episodes or are terminated thereby. Deficiency of vitamin A leads to metaplasia of the pulmonary epithelial lining with atrophy and keratinization favoring the development of pneumonia.

Shock and shock-like states, accompanied by a disturbance of the vasomotor system in the lungs, cause stagnation of the blood, congestion, edema, atelectasis and transudation into the alveoli and provide circumstances favorable for bacterial growth. Such changes occur in innumerable conditions, the more important of which are burns, poisoning, toxemia, heat exhaustion, trauma, surgical operation, electric and psychic shock. *Lung blast* or the concussion from the shock waves of a severe explosion may injure the lung and result in pneumonia.

Numerous gases, volatile substances and dusts encountered in industry and war predispose to pneumonia. Aspiration of foreign bodies or fluids into the airways or lung either cause obstruction and atelectasis or direct irritation of the pulmonary tissues. States of coma or paralysis of the nerves of deglutition or respiration from any cause favor the aspiration of secretions, vomitus or other foreign material which cause atelectasis and pneumonia. Sudden chilling of the body may cause transient ischemia of the mucous membranes of the respiratory tract and favor infection. Areas of atelectasis or of allergic pneumonia, if persistent, often are secondarily invaded by bacteria. Bacterial invasion may occur during therapy with adrenal steroids or with antimicrobics.

Clinical

The symptoms of secondary pneumonia of mixed infection obviously vary greatly. The age and condition of the patient, the nature and severity of the underlying or predisposing factors, the variety of bacteria operative and the extent of the lesion all modify the symptoms. The presence of cough, a little higher fever, a pulse rate and respiratory rate higher than usual, though they may be actually caused by a *pneumonia*, may be ignored during some other serious illness. Pneumonia may be present without causing any symptoms or abnormal physical signs. On the other hand, pneumonia may commence suddenly, dominate the picture and overwhelm the patient in a day or two.

In the average case, the patient gradually or suddenly becomes worse, or does not recover from his primary disease so rapidly as would be expected. Evidence of tracheitis and bronchitis may not appear. The pulse rate, respiratory rate and temperature show a tendency to rise and the patient *feels ill*. The skin may be hot and dry or there may be profuse sweating. A sensation of tightness in the chest and substernal pain occur. The cough may become more and more distressing and exhausting. Evidence of pneumonia is indicated by the severity of the constitutional reaction, an elevation of the pulse rate, respiration rate, the temperature and by physical and roentgenographic signs of newly developed pulmonary disease.

Fever may be absent or persistently high

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In the average case the patient gradually or suddenly becomes worse or does not recover from his primary disease so rapidly as would be expected Evidence of tracheitis and bronchitis may not appear The pulse rate respiratory rate and temperature show a tendency to rise and the patient feels ill The skin may be hot and dry or there may be profuse sweating A sensation of tightness in the chest and substernal pain occur The cough may become more and more distressing and exhausting Evidence of pneumonia is indicated by the severity of the constitutional reaction an elevation of the pulse rate respiration rate the temperature and by physical and roentgenographic signs of newly developed pulmonary disease

Fever may be absent or persistently high

but more often rises and falls as the process spreads from place to place in the lungs In patients who show no frank physical signs, a diagnosis of pneumonia often can be guessed at correctly from the irregular character of the fever chart It may last from a few days to several weeks and subsides by lysis Frequently, there is a recurrence of fever and symptoms Relapse or persistence of fever indicates activity of infection During bronchitis, any fever lasting longer than four days is suggestive of pneumonia

The pulse rate usually is increased but relatively less so than the respiration rate Respiration is affected roughly in proportion to the extent of pulmonary involvement and may reach 60 or 80 per minute, especially in children Tachypnea and dyspnea may be distressing Cyanosis usually is present Cough often is troublesome In infants and in the aged cough may be ineffectual and sputum either is not raised or is swallowed The sputum is variable, ranging from thin mucus to tenacious mucopus It may be pinkish, brown or bloody The quantity raised varies greatly

Frequently, especially in children, there is vomiting and anorexia Diarrhea is common The urine shows the usual changes resulting from fever There usually is leukocytosis In fatal cases, the pulse and respiration become feeble, cyanosis and apathy increase, tracheal rales appear and death from toxemia, exhaustion or asphyxia ensues

Physical Signs

The physical signs, like the clinical course, are variable The extent of the area over which signs are elicited may be small or may include the greater part of the chest Abnormal physical signs may be absent or may be obscured by the primary condition especially by malignant metastases, infarcts bronchiectasis, edema or asthma Physical signs vary from day to day, even from hour to hour, disappearing in one area to reappear later or fresh signs occur elsewhere in the lungs The spread of infection from place to place or temporary atelectasis caused by plugging of the bronchi with exudate are factors responsible for the rapid migration and variation of physical signs

Roentgenographic Signs

The roentgenographic appearance of the lungs in pneumonia of undetermined or mixed cause differs as widely as do the clinical and pathologic findings In general the shadows are not clearly defined In certain cases, shadows of pneumonia may be present without physical signs, less often physical signs may be present without demonstrable roentgenographic shadows There are usually small and irregular shadows of varying size scattered in both lungs The bronchovascular markings are intensified in proportion to the degree of peribronchial or perivascular inflammation In the pneumonias of certain infections, the lesions usually are denser near the hilum and in relation to the bronchovascular tree, in contrast with pneumonia resulting from shock, or from the aspiration of fluid, for in these the density occurs chiefly in the dependent portions of the lung

In the early period there may be few or no shadows cast on the film Patches of increased density may not be distinguishable from the normal markings or from pulmonary congestion Patches of consolidation may be hidden behind the heart or the domes of the diaphragm and may not be demonstrable with the usual technic In the majority of cases however, roentgenograms made at short intervals are valuable aids in registering the progression or regression of the lesion and, of course, in diagnosis.

Complications and Sequels

Pneumonia as discussed here is a complication or sequel of some primary condition Complications of secondary pneumonia, in turn, except in infants, are not so common as those observed in lobar pneumonia Bronchitis often is present Laryngitis and aphonia occassionally occur Endocarditis is rare, but pericarditis may result from direct extension of the inflammatory process from the lungs through the pleurae Small multiple lung abscesses may occur, especially in prolonged cases, and gangrene, though rare, may follow

As sequels, abscess, fibrosis, emphysema or

bronchiectasis may be mentioned Pulmonary osteoarthropathy rarely occurs

Diagnosis

In secondary pneumonia the variability of causes the insidious onset irregular course and physical signs often present difficulties in diagnosis A diagnosis of pneumonia often can be presumed from vague but suggestive signs or symptoms and its relative frequency in certain conditions As mentioned previously it sometimes is impossible to decide when bronchitis becomes pneumonia but when rales dyspnea and cyanosis are present when fever lasts longer than four days and when constitutional symptoms are considerable pneumonia must be suspected

The leukocyte count usually is increased Leukopenia may be present during the pneumonia accompanying typhoid fever typhus fever influenza in fulminating pneumonia of any form and in debilitated persons

Prognosis

The mortality varies depending upon many factors Obviously pneumonia is most often fatal for patients who are weakened by some other severe or prolonged disease and in malnourished or obese children. In later life chronic diseases often are terminated by pneumonia and the prognosis accordingly is bad The presence of bacteremia is a serious omen The depth of cyanosis and the frequency and weakness of the pulse are indications of the gravity of the infection It is generally true also that more widespread the involvement the worse the chances are for recovery The prognosis improved after the advent of antimicrobial therapy

Prophylaxis

Factors which reduce the incidence or severity of influenza colds measles pertussis typhus and so forth will automatically reduce the incidence of secondary pneumonia But in the actual presence of such primary diseases or in the other chronic diseases mentioned above much can be done to avoid pneumonia The patient while ill or during convalescence should be kept in bed for a reasonable time at least for several days after the temperature returns to normal He should at all times be protected from chilling and isolated from those suffering from mild infections of the respiratory tract It is needless to mention the importance of sufficient nourishment and of hygiene both general and oral The teeth and gums should be cleansed daily Pyorrhea gingivitis and other oral or dental disease should be treated The debilitated and the aged should be protected from the cold especially in inclement windy and dusty weather Slight respiratory tract infections should be noted immediately and the patient put to bed Severe colds pharyngitis laryngitis and bronchitis should never be considered lightly The danger of the spread of the infection downward is ever present and often can be prevented by sensible care

Normal persons with respiratory tract infection should not be anesthetized for elective surgical operations Should delay be unavoidable it is best to turn the patient s head to one side or lower it to prevent the aspiration of infected nasal and oral secretions during anesthesia Local anesthesia should be used if possible Secretions in the throat may be aspirated with a suction tube or removed with a swab The stomach should be empty to minimize vomiting

Depending on the clinical condition deep breathing induced by instruction or by the inhalation of 5% carbon dioxide gas may aid in preventing atelectasis and aid in the expulsion of sputum The patient s position in bed after an operation should be changed frequently An upright position or even placing the patient in a comfortable chair may be desired During nasal or oral surgical operation care should be taken to avoid accidental aspiration of blood pus saliva amputated tissue or extracted teeth Persons in coma from other causes or those in whom the muscles of deglutition and of the pharynx are paralyzed should be placed so as to permit secretions to drain through the mouth or sucked out with a vacuum pump Children should be instructed not to carry small objects (coins buttons safety pins peanuts etc) in their mouths Patients in shock from any cause particularly after accidents out-of-doors or after submergence in water should be taken

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The leukocyte count usually is increased Leukopenia may be present during the pneumonia accompanying typhoid fever typhus fever influenza in fulminating pneumonia of any form and in debilitated persons

Prognosis

The mortality varies depending upon many factors Obviously pneumonia is most often fatal for patients who are weakened by some other severe or prolonged disease and in malnourished or obese children In later life chronic diseases often are terminated by pneumonia and the prognosis accordingly is bad The presence of bacteremia is a serious omen The depth of cyanosis and the frequency and weakness of the pulse are indications of the gravity of the infection It is generally true also that more widespread the involvement the worse the chances are for recovery The prognosis improved after the advent of antimicrobial therapy

Prophylaxis

Factors which reduce the incidence or severity of influenza colds measles pertussis typhus and so forth will automatically reduce the incidence of secondary pneumonia But in the actual presence of such primary diseases or in the other chronic diseases mentioned above much can be done to avoid pneumonia The patient while ill or during convalescence should be kept in bed for a reasonable time at least for several days after the temperature returns to normal He should at all times be protected from chilling and isolated from those suffering from mild infections of the respiratory tract It is needless to mention the importance of sufficient nourishment and of hygiene both general and oral The teeth and gums should be cleansed daily Pyorrhea gingivitis and other oral or dental disease should be treated The debilitated and the aged should be protected from the cold especially in inclement windy and dusty weather Slight respiratory tract infections should be noted immediately and the patient put to bed Severe colds pharyngitis laryngitis and bronchitis should never be considered lightly The danger of the spread of the infection downward is ever present and often can be prevented by sensible care

Normal persons with respiratory tract infection should not be anesthetized for elective surgical operations Should delay be unavoidable it is best to turn the patient s head to one side or lower it to prevent the aspiration of infected nasal and oral secretions during anesthesia Local anesthesia should be used if possible Secretions in the throat may be aspirated with a suction tube or removed with a swab *The stomach should be empty* to minimize vomiting

Depending on the clinical condition deep breathing induced by instruction or by the inhalation of 5% carbon dioxide gas may aid in preventing atelectasis and aid in the expulsion of sputum *The patient s position in* bed after an operation should be changed frequently An upright position or even placing the patient in a comfortable chair may be desired During nasal or oral surgical operation care should be taken to avoid accidental aspiration of blood pus saliva amputated tissue or extracted teeth Persons in coma from other causes or those in whom the muscles of deglutition and of the pharynx are paralyzed should be placed so as to permit secretions to drain through the mouth or sucked out with a vacuum pump Children should be instructed not to carry small objects (coins buttons safety pins peanuts etc) in their mouths Patients in shock from any cause particularly after accidents out-of doors or after submergence in water should be taken

to a warm, dry place as soon as possible and treated with appropriate measures

The excision of tonsils is of no value as a prophylactic measure in preventing pneumonia

Prophylactic vaccination against the bacteria commonly found in the normal throat is of no value in preventing secondary pneumonia

Prophylactic Use of Antimicrobics

The advisability of the routine use of antimicrobics to prevent pneumonia during other disease or surgical operations is controversial Generally, indiscriminate prophylactic efforts are not recommended because of the danger of sensitizing patients to a therapeutic agent which may be urgently needed later, because of unpleasant side effects incident to the use of antimicrobics and of the danger of superinfection It seems wiser to reserve therapy until pneumonia is suspected or present When special conditions demand the prevention of pneumonia, penicillin in amounts of 100,000 units (120 mg) or more intramuscularly twice daily may be given over the critical period to attempt to control the bacteria chiefly responsible On the other hand because of the likely presence of mixed infection an antimicrobic with a broader antibacterial spectrum such as tetracycline, erythromycin or chloramphenicol may be preferable except for the unpleasant gastrointestinal intestinal disturbances they may cause and of their cost

Treatment

Symptomatic treatment is the same as for other forms of pneumonia The selection of the appropriate antimicrobic may be difficult Penicillin is the agent of choice if infection is dominated by pneumococci, staphylococci or hemolytic streptococci For mixed infection, the obvious selection is an antimicrobic of broad antibacterial action such as one of the tetracyclines, erythromycin or chloramphenicol

SPECIAL FORMS OF SECONDARY PNEUMONIA

Because of their frequent occurrence and of the special factors which lead to their development, several forms of secondary pneumonia are important enough to consider separately as follows

POSTOPERATIVE PNEUMONIA

The incidence of significant pneumonia and atelectasis after surgical operations is variable It is higher after surgery in the upper part of the abdomen In one series it was 7 6%, but after an improvement in management, the incidence fell to about 5% [1] Whether general anesthesia or spinal anesthesia is employed makes little difference in patients properly cared for The incidence is higher in men, in smokers, in patients with acute or chronic infection of the respiratory tract, with increasing age and in proportion to the duration of the operation Postoperative pneumonia is caused by a combination of factors, among which chiefly are an elevation of the diaphragm, aspiration of secretion after anesthesia that obliterates the cough and swallowing reflexes, the formation of bronchial plugs, thrombosis or embolism of pulmonary vessels, atelectasis and shock

It is difficult often to differentiate infarct, atelectasis, bronchitis and pneumonia The signs and symptoms may be identical Any of the conditions named may begin shortly after operation or a day or two later Pneumonia in particular is characterized by cough with sputum, a sensation of tightness or pressure in the chest, tachypnea, dyspnea, tachycardia, fever and leukocytosis, in varying combinations In some cases, the only evidence of pneumonia may be fever, rales and an abnormal roentgenographic shadow in the lung The lower lobes usually are affected

Prevention

Postoperative pulmonary complications can be kept at a minimum by proper care before, during and after operation Unless an emergency exists, surgery should be avoided in the presence of infection of the respiratory tract

however mild. Patients with chronic pulmonary disease should evacuate as much secretion as possible before operation. The teeth and mouth should be clean. During operation anesthesia should be as light as possible for the task at hand. Regurgitation and aspiration of vomitus must be guarded against. After operation the patient should be turned at least every hour. Secretions or vomitus in the nose and oropharynx if present must be removed. Inhalation of carbon dioxide gas briefly two or three times an hour for about 6 hours after operation increases the depth of respiration and aids in the expulsion of secretion. Gastric suction tubes if used should be removed as soon as possible to avoid nasal and pharyngeal irritation but suction may be needed if the stomach or bowel are distended. Antimicrobics should not be used routinely for prophylaxis. If there is any reason to suspect bacterial infection or if it is imperative for various reasons these agents may be used prophylactically. According to Hoerr antimicrobics have little if any value when given prophylactically. Pulmonary complications in some patients developed while penicillin was being given. It is of greater importance to control the mechanical factors to prevent postoperative pneumonia.

Treatment

The essential management in most instances is directed toward correcting atelectasis. It includes frequent change of position or change to an upright position, avoidance of restrictive abdominal or thoracic binders or bandages, control of abdominal distention and aspiration of oropharyngeal or tracheal secretions and according to some investigators periodic inhalation of carbon dioxide. When evidence of pneumonia is present antimicrobic therapy according to cause is necessary. Pneumococci are the chief pathogens.

ASPIRATION AND DEGLUTITION PNEUMONIA

Solids or fluids may enter the bronchi and lungs as a result of some interference with the normal expulsive mechanism. The foreign substance serves both as an irritant which incites inflammation and as an obstruction which prevents drainage thereby causing atelectasis or infection. Oropharyngeal secretions which contain pathogenic bacteria are carried into the lungs and retained with the aspirated material thus providing the infective agents which cause pneumonia. There may be no associated bronchitis.

This form of pneumonia is apt to follow the aspiration of secretions during coma from any cause such as shock, sunstroke, uremia, general anesthesia and various forms of poisoning, the aspiration of water during submersion, the aspiration of vomited gastric contents or of blood, pus or amniotic fluid, the entrance of foreign bodies into the trachea and bronchi, aspiration of secretions during paralysis of the muscles of deglutition caused by encephalitis, poliomyelitis, bulbar palsy, tetanus, rabies and local anesthesia. The accidental aspiration of silver proteinate, zinc sulfate and tannic acid often used by rhinologists must be mentioned. The form of pneumonia resulting from the aspiration of oil into the lungs is described in a separate section.

The resultant pneumonia usually is caused by mixtures of microorganisms and is complicated by the presence of a foreign body or by fluid. The pathologic changes are varied and usually are accompanied sooner or later by suppuration and abscess formation. The symptoms and signs of pneumonia usually begin within a few hours after the substance enters the bronchi or lungs. The prognosis depends upon the extent of the primary pulmonary damage, on the nature of the aspirated substance and of the subsequent infection, on the severity of the primary condition and on the age and condition of the patient.

Treatment

Besides treating the general condition, bronchoscopic aspiration of fluids or removal of foreign bodies may be necessary. The pneumonia is treated as described for mixed infection, page 180.

TRAUMATIC PNEUMONIA

Severe blows to the chest wall with or without fracture of ribs or external evidence of

contusion account for about 2 or 3% of pneumonias treated in hospitals[3] The commonest causes are falls, blows from flying or falling objects, traffic and aviation accidents and concussion (lung blast) by air pressure waves from a severe explosion Direct penetration of the lung by weapons, missiles, fractured ribs and by other causes is not considered here The lungs may be injured by direct violence to the thorax by sudden compression or nipping between the chest wall and liver or spleen, and by contrecoup, that is, in an area distant from the site of impact or in the opposite lung Contusion of the pleurae and subsequent fibrinous pleuritis occurs

Injured persons without thoracic trauma may develop pneumonia from the general shock itself, from aspiration during unconsciousness or anesthesia, from aspiration of vomitus or from hypostasis[4] Fracture of the bones of the thorax and puncture of the lung may be present The injured lung shows a variable amount of subpleural ecchymosis or a hematoma, atelectasis, laceration of the alveoli, capillaries and supportive tissue, and later hemorrhagic consolidation under the site of injury or distant from it Extensive lesions may leave cavities Pneumothorax, hemopneumothorax and emphysema of the skin or mediastinum may be present Actual pneumonia, that is, infection of the area of injury may not occur The injured pulmonary tissue, however, provides a favorable medium for the growth of any bacteria which happen to reside in the respiratory tract In one series of cases, pneumococci of the high numbered types were the chief invaders[5]

Traumatic pneumonia begins within a few days after the injury If pneumonia develops later than six days, its direct relationship to trauma is questionable If pneumococci alone are the cause, the typical clinical lobar form may occur Some pneumococcic infections give rise to atypical pneumonia and mixed infection always does In Phillips' cases, the pneumonia simulated that of mild to moderately severe pneumococcic pneumonia Bacteremia seldom occurred and recovery took place within a week in half of the patients Empyema occurred in two It often is difficult to decide if pneumo[illegible] [illegible]lly present, and if so when it begins The symptoms and signs of atelectasis or of pulmonary contusion with a sterile hemorrhagic area in the lung are similar to those of pneumonia

Prevention

Patients likely to develop traumatic pneumonia should receive promptly an intravenous injection of 0 4 mg ($^1/_{50}$ grain) of atropine sulfate and 30 mg ($^1/_2$ grain) of papaverine hydrochloride to retard the vagal reflex which leads to bronchospasm, hypersecretion, atelectasis and edema The dose should be repeated every four hours for two days after injury Oral therapy may be substituted but it is not as dependable The matter of giving antimicrobics prophylactically to all patients with injured thoraxes is controversial Much depends on clinical judgment If used, penicillin is the agent of choice but tetracycline or others may be given orally and cover a broader range of bacterial infection Atelectasis may be prevented by changing the patient's position, by enforced deep breathing or by inhalation of carbon dioxide gas

Treatment

The pneumonia is treated in the usual manner described on page 150 It is important not to restrict respiration by the application of adhesive tape or other thoracic binders Injection of anesthetic agents locally at the site of fracture to control pain, if present, is preferable Pleural pain may be relieved by injecting solutions of procaine Sedatives and narcotics should be used minimally or not at all Shock, hemorrhage and other associated conditions must be corrected Atelectasis may be relieved by inhalations of carbon [illegible] oxide, deep breathing and control[illegible] coughing

PNEUMONIA IN INFANTS

The majority of cases of pneumonia in [illegible]fancy occur in the first 2 years of life Th[illegible] are induced by the feebleness or und[illegible] [illegible]nt of the protective mechanis[illegible] at this age, and often are caused [illegible] of fluid Prematurity, malnutritio[illegible] [illegible]nd [illegible]ections and disorde[illegible]

all predispose to pneumonia[5] The bacteria most frequently found in the lungs are pneumococci staphylococci streptococci and influenza bacilli As might be expected mixed bacterial infection usually is the cause While antimicrobic therapy has reduced the mortality rate in infants the reduction is not so great as in adults At present the therapeutic limits of effective antibacterial therapy seem to have been reached Any further improvement must come from other methods of therapy to establish and support the resistance of the host

SENILE PNEUMONIA (ASTHENIC AND TERMINAL PNEUMONIA)

Pneumonia in old age may be clinically characteristic of the kinds caused by various agents as discussed elsewhere in this chapter or because of the infirmities of age it may not assume its distinctive form The term *senile pneumonia* as used here implies pulmonary infection which Osler referred to as the friend of the aged It may be difficult to decide in some instances whether the patient died from pneumonia or if pneumonia occurred because dissolution was under way The enfeeblement of old age like that of early infancy is conducive to the development of pneumonia The presence of degenerative cardiovascular renal lesions chronic pulmonary disease or other infirmities increases the liability to pneumonia In many cases a slight infection of the respiratory tract is all that is necessary to initiate pulmonary invasion As they trickle down the trachea and bronchial tree secretions which in robust persons would be expelled enter the lungs and incite inflammation with the mixture of organisms which they carry with them In some instances inflammation of the upper air passages spreads downward by continuity until the bronchioles and alveoli are involved In a few the infection appears to start primarily in the bronchioles or lungs Pneumococci almost always are found staphylococci streptococci and other forms frequently are present in various combinations In one series of 166 cases a single bacterium was present in 73 cases (the pneumococcus usually of type III in 65) 13 apparently were of viral origin and in the rest the cause was undetermined[6] The character of the lesion often is nonspecific with areas of atelectasis edema and suppuration

Symptoms

The onset of pneumonia is insidious with low fever and few pathognostic signs There is an apparent diminution or absence of nervous tone Prostration may be the only complaint Chills seldom occur Cough if present is feeble and sputum may not form or cannot be raised because of weakness The pulse rate and respiratory rate usually are increased and there may be low delirium or stupor which gradually deepens until death occurs Recovery may ensue The leukocytes may not be increased The whole picture suggests the enfeeblement of the forces usually operative in combating infection Hiccough and abdominal distention often resist all forms of treatment The physical signs are dullness rales and changes in the breath and voice sounds in the areas involved but they often are obscured by signs of pulmonary congestion and tracheal rales incident to failing circulation Roentgenography is helpful in diagnosis Pneumonia may be discovered only at necropsy[7]

The treatment is essentially the same as that described on page 150 Antimicrobic therapy has lowered the mortality rate but as in young infants it still is considerably higher than during middle life Further improvement in the mortality rate depends on the development of means to prevent pneumonia and to increase the resistive ability of the host

CHRONIC PNEUMONIA

Chronic or unresolved pneumonia as such is a rare condition which in some patients persists for weeks or months after an acute pulmonary infection The terms should not be confused with delayed resolution which implies slow resorption of the results of pulmonary inflammation after any form of pneumonia in a person who is otherwise well In many instances of chronic pneumonia some underlying condition is present like bronchiec

tasis abscess foreign body or tumor surrounded by areas of inflammation which persist or recur at short intervals Chronic pneumonia may be caused by any of the usual bacteria or by M tuberculosis fungi and by long exposure to bagasse or beryllium

Pulmonary Adenomatosis is a chronic disorder resembling a disease in sheep called jagziekte[8] It occurs most often in late adult life The cause is unknown but is thought either to be infectious or neoplastic in nature

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PNEUMONIAS NOT CAUSED BY INFECTION

OIL ASPIRATION PNEUMONIA

(Lipoid Cell, Lipid Pneumonia)

This pulmonary disease was described by Laughlen in 1925 Oils or fats enter the lung during various procedures and circumstances namely (a) after nasal instillation with an *atomizer or a medicine dropper* (b) during attempts to feed oil or fat forcibly to persons who resist and refuse to swallow (c) by regurgitation from the esophagus into the trachea and (d) by the local formation of cholesterol esters In healthy persons the expulsive mechanism of the lungs and bronchi removes foreign *substances which happen to* enter but in the case of bland oils the cough reflex may not be stimulated and in debilitated persons irritability is reduced Liquid petrolatum milk fat and cod liver oil are most commonly the cause of lipoid cell pneumonia because of their wide use as a base for medicated *nasal sprays and for nutritive purposes* Cod liver oil egg yolk lard cream and other animal fats cause a greater reaction in the lung than liquid petrolatum castor oil olive oil or poppy seed oil Either the oils themselves or the fatty acids formed by hydrolysis of animal and vegetable oils act as irritants and *stimulate the* accumulation of macrophages giant cells and eventually of fibrous tissue

Lipoid pneumonia was reported in from 2 to 25% of children and in 15% of chronic bedridden adults studied at necropsy[10] Lipoid pneumonia also is found in otherwise healthy adults who habitually spray liquid petrolatum into the nose or throat or take it habitually for constipation It occurs in the demented the aged or others who for various reasons regurgitate and aspirate food *It is caused occasionally* by iodized oil used for bronchography but is of no significance Trouble occurs chiefly when small amounts of the offending agent enter the lung repeatedly over a long time The pneumonia often is asymptomatic and is detected during mass roentgenographic surveys *of normal people or at necropsy*

An intrinsic form of lipoid cell pneumonia occasionally occurs in patients in whom oil or fat have not been aspirated Cholesterol esters form and accumulate in degenerating pulmonary tissue especially when the lungs *have been irradiated*[3]

The various forms in which lipoid cell pneumonia occurs may be listed as follows I The asymptomatic form which is discovered at necropsy or during physical or roentgenographic *examination II The symptomatic* form as (a) acute or chronic pneumonia (b) recurrent transient pulmonary disease (c) low grade bronchitis (d) simulating pulmonary neoplasm with cough pain and roentgen

shadow and (e) in clinical states favoring aspiration such as bulbar palsy multiple sclerosis debility etc

Pathology

The immediate effects of oil injected experimentally into the lung are those of mechanical obstruction of a group of alveoli or lobules Inflammation with accumulations of mononuclear cells occurs within a few minutes after oil reaches the lung The degree of inflammatory reaction varies greatly and depends upon the nature of the oil the amount present the duration of its presence and the ability of the tissues to react There are localized hemorrhages and edema which soon subside unless the oil is highly irritating or repeatedly introduced in large amount Cod liver oil produces the most severe reaction with intense fibrinous infiltration and even necrosis After two weeks the bronchiolar epithelium proliferates and later the oil is changed by hydrolysis into an insoluble substance which provokes the accumulation of giant cells The oil or its residue may be removed from the lung partly by expectoration in sputum partly in the lymphatics by exportation and partly by encystment and digestion

Grossly the lesions are areas of patchy pneumonia with special characteristics such as a lumpy sensation on palpation and a rubbery consistency Pleurisy is not present unless as a complication The cut surface is dry or may be oily depending upon how recently the oil or fat gained entrance and upon how much is present Yellow or brown irregular patches of peribronchial consolidation are present often sharply demarcated from normal pulmonary tissue In long standing cases the pathologic and normal areas may merge and in others abscess cavities of various size atelectasis and fibrosis may be present Yellow tumor like nodules may be present The picture is modified if secondary infection has occurred

Microscopically the reaction is similar to that evoked by other foreign material It is inflammatory in nature and consists of an exudate in the alveoli alveolar and bronchiolar walls and elsewhere made up of cells whose purpose it appears is to engulf the oil globules and transport them to the lymphatics for removal The cells for the most part are large phagocytic monocytes Plasma cells polymorphonuclear cells eosinophiles and giant cells also may be present in varying proportion The alveoli may contain free fat or are packed with mononuclear cells full of fat globules The alveolar walls especially in older lesions may be thickened and fibrotic In late cases fibrous tissue usually is present as an end result of the inflammatory process Granulomas composed of the cells just named may become surrounded with layers of epithelial cells and fibroblasts to form cysts The lymphatics may be blocked with masses of free oil or fat and cells containing fat globules If the process developed slowly by small constantly added increments of oil lesions of varying ages are present

Symptoms

The symptoms of oil aspiration pneumonia vary greatly depending upon the amount and the kind of oil or fat aspirated and on the age and general condition of the patient In the usual forms in which small amounts of oil enter the lung at short intervals over long periods the symptoms of pneumonia are absent or so mild as to escape detection Furthermore since many infants who receive oil have other diseases these usually dominate the picture and respiratory tract symptoms if present are ignored or attributed to other cause In many patients the onset is insidious and a rapid respiration rate and low grade illness may be the only clinical evidence to suggest the condition Dyspnea hacking cough and low grade fever frequently are noted There may be no fever If a large amount of oil is aspirated at once there will be the usual evidence of foreign matter in the lung with cough and dyspnea

The physical signs often are minimal and not in proportion to the extent of the pulmonary lesion There may be dullness over the affected areas which usually are near the hilum and in the dependent parts of the upper and lower lobes but portions of normal lung over the pneumonic areas may yield a normal percussion note The breath sounds may be un

altered or harsh or tubular sounds may be heard depending upon the degree of consolidation and its nearness to the periphery of the lung. Rales often are present. Acropachy occurs in some patients.

The disease usually lasts for months or years. Recovery slowly may take place in uncomplicated cases if no more oil gets into the lung, and if the damage is not too great, but often chronic fibrosis, abscess with cavitation, cysts or calcification result. Death may occur from secondary bacterial invasion of the lungs or from exhaustion or asphyxiation by obliteration of lung tissue.

Diagnosis

The disease always should be suspected in small, debilitated infants who fail to gain and who received and perhaps resisted, feedings of cod liver oil, milk, cream or egg-yolk, or who have had oil placed in the nares for various reasons. The symptoms mentioned above are suggestive of the diagnosis. In adults, a history of using oil in the nose continually or of repeatedly regurgitating food or taking liquid petrolatum over long periods, is of importance. In uncomplicated cases, there is no fever and the number of leukocytes is normal. The sputum, if any, or secretions aspirated during bronchoscopy may contain free or phagocytosed oil globules visible microscopically and made prominent by special stains for fat. The identity of the causative agent and the age of the lesion may be determined by their fluorescence under ultraviolet light.[4] The disease often is unsuspected during life and is found incidentally or at necropsy.

Roentgenography aids in recognizing the condition and to show its location and extent. Shadows of varying density may be seen in different parts of the lung, usually near the hilum and in the dependent portions. Some areas may be so dense as to suggest calcification, and around them may be the lucency of normal lung substance. The decrease of density toward the periphery and predominance of involvement in the dependent posterior or dorsal lobar regions as revealed by making lateral plates, are of diagnostic importance. When the process is extensive, the right side is involved more than the left, the upper lobes more than the lower. The mediastinal lymph nodes seldom are enlarged, nor are the bronchovascular shadows thickened.

Pulmonary tuberculosis, sarcoidosis, fungal infection, atelectasis, tumor or syphilis of the lung must be considered in differential diagnosis. In several instances lobectomy was performed for suspected cancer.

Prophylaxis

Oily substances should not be placed in the nose for nasal medication. Care must be taken that liquid petrolatum given for laxative purposes is not regurgitated and aspirated into the trachea. Since, in many cases, lipoid cell pneumonia occurs in infants who struggle and cough when given cod liver oil, milk or other fat containing foods, it is obvious that care should be taken to prevent the entrance of such substances into the trachea.

In older children or in adults who are ill, comatose, or whose pharyngeal and cough reflexes are modified by some neurologic disorder unusual care must be taken during feeding. When vomiting occurs, patients should be turned on the side or placed so that drainage into the lung is avoided. Habitual use of liquid petrolatum to correct constipation should be abandoned.

Treatment

Treatment is directed chiefly to correcting a primary disorder, if present, and in the prevention of access of any more oil or fat into the lung, otherwise it is largely symptomatic and supportive. Lobectomy may be indicated.

PNEUMONIA CAUSED BY INHALATION OF HYDROCARBONS

Aspiration of kerosene, gasoline, fuel oil and other oils in their fluid or volatile state causes pneumonia of varying degree of severity depending on the age of the patient, and the kind and amount of the offending agent which enters the lung.[5]

The immediate effects of the ingestion or inhalation of irritating oils are burning of the mouth and throat, spasm of the glottis, severe coughing, vomiting, choking and retrosternal

or epigastric pain Later symptoms are those of severe intoxication shock and coma ending occasionally in death The pulmonary symptoms are those of acute pneumonia The lesions are characterized by bronchial and peribronchial necrosis edema congestion hemorrhage, fibrinous exudate and macrophage lymphocytic infiltration

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RADIATION PLEUROPNEUMONIA

Radiation pleuropneumonia is the name given to lesions in the lung and pleura caused by high voltage roentgen therapy applied to the thorax for various purposes The entity was first described by Christie and his associates in 1922 It is found chiefly in patients with malignant disease of the breast or lymphomatous disease who are treated with massive doses of roentgen rays With the change in methods of treatment by using the fractionated irradiation high voltage may be applied without much injury to the skin but a greater amount of damage to deep structures results The pulmonary lesion usually develops directly in the path of radiation A slight degree of pleural thickening or pulmonary fibrosis may result from such treatment but actual pneumonitis and pleurisy with effusion may follow When under these circumstances evidence of pulmonary disease is detected it is often mistaken for a spread of the malignant process to the lung or for tuberculosis The lesions may disappear after several weeks or months provided no further roentgen ray treatment is applied Occasionally death occurs from rapidly developing pulmonary insufficiency [1]

Persons differ greatly in susceptibility to the effects of roentgen rays Some develop evidence of pleurisy or pneumonia after a few treatments some after prolonged high voltage therapy and others are unaffected For the most part it appears that milder forms of radiation pleuritis or pneumonia are symptomless and cannot be recognized unless roentgenograms are made at short intervals In one series of cases only in 3 patients out of 45 did the symptoms and signs call attention to the pneumonic process

Pathology

In one patient studied at necropsy the lung in the affected area was bound to the chest wall by loose adhesions The lung was covered with a sticky greenish exudate and the pleura was thickened The affected lobe was solid and the interlobar pleura was a dense fibrous band There were peculiar dense patchy dull white areas many of which were in close relation with the bronchi Diffuse peribronchial fibrosis was present Microscopically the alveolar walls were thickened and there was exfoliation of the epithelium Perivascular and peribronchial thickening was prominent

In animals exposed to high voltage roentgen rays two main types of changes were observed one was early and acute characterized by edema and congestion the other was late with fibrosis and atelectasis In the early stages the air sacs were filled with coagulated exudate and desquamated epithelium In all cases thickening of the alveolar walls was present and the air spaces were compressed and often obliterated

Symptoms

The lesion usually is symptomless and undetectable except by roentgenography Actual symptoms when they appear develop 1 week or more after exposure to roentgen rays and resemble those of an acute mild infection of the respiratory tract The onset may be sudden with pleuritic pain and an irritating dry cough Dyspnea on exertion and cyanosis may be noted Fever may be absent unless

bacterial invasion takes place The physical signs are indefinite but in the early stage there may be dullness, decreased tactile fremitus, diminished breath and voice sounds and rales Later the signs are those of atelectasis and fibrosis, with retraction of the mediastinum and diaphragm toward the affected side Roentgenograms show evidence of fairly well localized infiltration which easily is mistaken for the common forms of pneumonia The shadow is mottled and evidence of pleural thickening and of effusion often is present The shadow either disappears after several weeks or months or is permanent as the result of fibrosis The leukocytes are normal in number or reduced as a result of irradiation particularly the lymphocytes

Diagnosis

When signs and symptoms of pulmonary disease appear in patients with malignant neoplasms who have had high-voltage roentgen ray treatment applied to the thorax, it may be difficult to tell whether (a) there has been metastasis or direct extension of the neoplasm into the lung, (b) the patient has pneumonia of bacterial origin, (c) the lesion is caused by irradiation, or (d) a combination of these conditions is present The absence of sputum, high fever and leukocytosis aids in ruling out the usual forms of pneumonia The roentgenographic appearance and distribution of the density in the lung may aid in differentiating malignancy from radiation pneumonia, but the most helpful evidence is the spontaneous diminution or disappearance of the lesion after several weeks or months provided no further irradiation is applied

There is no treatment except to stop irradiation or, if irradiation must be continued, to prevent further injury by protecting the involved area of the lung from the rays with shields or by directing the rays from a different angle

Therapy with cortisone and corticotrophin may cause temporary symptomatic improvement

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ALLERGIC PNEUMONIA, LOEFFLER'S SYNDROME, PULMONARY EOSINOPHILIA

Transitory infiltration of the lung with eosinophilic cells is believed to be the result of the reaction of lung tissue after exposure to any one of a variety of antigens against which the lung was previously sensitized The reaction can be induced experimentally in animals by sensitizing them to eggwhite, for example, and injecting the same antigen intratracheally after the proper time interval In man, eosinophilic reaction and infiltration occur in other tissues of the body in allergic states and it is surprising that involvement of the lung was unrecognized until it was described in 1932 by Loeffler Transient pulmonary eosinophilia and eosinophilia of the blood occurs at times during allergic rhinitis, urticaria and asthma Similar reactions are noted in some patients with amebiasis, ascariasis, trichiniasis, schistosomiasis, ancylostomiasis, cutaneous helminthiasis and other parasitic infections They are not to be confused with the pulmonary reaction incident to the passage of some of these parasites through the lung during a stage in their life cycle as described on page 175 Eosinophilic pulmonary reaction with or without eosinophilia in the blood occurs at time during tuberculosis, brucellosis, coccidioidomycosis and probably in other chronic infections and has occurred during sulfonamide therapy In many cases the cause is unknown The pulmonary lesion is similar to that found in polyarteritis (periarteritis nodosa) and, as described later, in tropical eosinophilia

Pathology

Little is known of the pathologic changes because the disease seldom is fatal A patient who had had "asthma" for 7 years and died in an acute attack of allergic pneumonia was studied at necropsy [1] The lungs showed advanced organization and a widespread alveolar and bronchial exudate, a predominance of eosinophilic cells and scattered patches of granulomatous inflammation There were

thickening of the blood vessels and perivascular infiltration suggestive of polyarteritis. In other reported cases the pneumonic exudate was not organized.

Clinically the disease usually is mild and of short duration with recurrences at short or long intervals. Severe and fatal cases have been observed. In the average case the symptoms are those of fatigue, annoying cough, sometimes pain in the chest and scanty sputum. Asthma-like attacks may occur. The temperature is normal or slightly elevated. The sedimentation rate is increased slightly. There are exaggerated breath sounds and rales over the areas of infiltration which within hours come and go or move from place to place. Abnormal signs also arise from areas of atelectasis. Pleural effusion seldom occurs. The leukocytes are normal or increased in number. Eosinophilia of from 6 to 70% accompanies the pulmonary signs. The sputum may be purulent and contains eosinophilic cells in predominance. The characteristic feature is the fleeting, migratory nature of the pulmonary changes detectable clinically and especially roentgenographically. One or both lungs may be involved. Roentgenographic shadows often are greater than one would suspect from physical examination. Fleecy or dense areas may appear, disappear and reappear in a few days and recur in different areas for several weeks.

Diagnosis is made on the basis of the description just given and the frequent coexistence of the allergic conditions or of the diseases mentioned. The presence of underlying disease such as one of the parasitoses, asthma and the other disorders listed previously may be confusing. Pulmonary tuberculosis, viral pneumonia and atelectasis most frequently are suspected. Early diagnosis is essential to avoid recurrences and secondary infection and to prevent subsequent irreversible fibrotic changes in the lung.

Treatment

Most important is the detection of the specific allergen or disease which causes the pulmonary reaction. Removal of the cause prevents further trouble. For mild attacks no treatment is needed. In severe cases transient relief may be afforded by injections of epinephrine hydrochloride. Antihistaminic drugs seldom are effective. Striking improvement was reported in a severe case by the injection of 35 mg. of adrenocorticotropic hormone given every 6 hours for 6 days and 10 mg. doses for several more days. A relapse a month later again was controlled by corticotrophin.[3]

TROPICAL PULMONARY EOSINOPHILIA

As mentioned in the preceding section, the relationship of this disorder to allergic pneumonia is uncertain. Many features are common to both diseases but there are differences. The condition had been noted since 1923 and was established as an entity by Frimodt-Moller in 1940. Most of the cases were observed in India. Numbers of cases were observed in American military personnel in the tropics during the war.

In tropical eosinophilia the onset is said by some to be sudden with fever which lasts a few weeks and may become chronic. Splenomegaly and generalized adenopathy are present. Most difficult to explain is the beneficial effect reported after the therapy with arsphenamine compounds. According to Ball the onset is insidious with wheezing, cough and mucoid sputum. Cough may be violent and paroxysmal. The attacks last a few days but recur in increasing severity and duration. The disorder may recur for years. Pain in the chest and hemoptysis occur as prominent features but fever is low or absent in most cases.[1] Otherwise the signs and symptoms are the same as those in allergic pneumonia.

Therapy with arsenicals is said to relieve the condition in about 50% of cases. Mapharsen is the agent of choice. A Herxheimer-like reaction may occur. Therapy with adrenocorticotrophic hormone had no effect in one case.[4] Symptomatic treatment is the same as for allergic pneumonia.

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bacterial invasion takes place. The physical signs are indefinite but in the early stage there may be dullness, decreased tactile fremitus, diminished breath and voice sounds and rales. Later the signs are those of atelectasis and fibrosis with retraction of the mediastinum and diaphragm toward the affected side. Roentgenograms show evidence of fairly well localized infiltration which easily is mistaken for the common forms of pneumonia. The shadow is mottled and evidence of pleural thickening and of effusion often is present. The shadow either disappears after several weeks or months or is permanent as the result of fibrosis. The leukocytes are normal in number or reduced as a result of irradiation, particularly the lymphocytes.

Diagnosis

When signs and symptoms of pulmonary disease appear in patients with malignant neoplasms who have had high voltage roentgen ray treatment applied to the thorax it may be difficult to tell whether (a) there has been metastasis or direct extension of the neoplasm into the lung, (b) the patient has pneumonia of bacterial origin, (c) the lesion is caused by irradiation, or (d) a combination of these conditions is present. The absence of sputum, high fever and leukocytosis aids in ruling out the usual forms of pneumonia. The roentgenographic appearance and distribution of the density in the lung may aid in differentiating malignancy from radiation pneumonia, but the most helpful evidence is the spontaneous diminution or disappearance of the lesion after several weeks or months provided no further irradiation is applied.

There is no treatment except to stop irradiation or, if irradiation must be continued, to prevent further injury by protecting the involved area of the lung from the rays with shields or by directing the rays from a different angle.

Therapy with cortisone and corticotrophin may cause temporary symptomatic improvement.

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ALLERGIC PNEUMONIA, LOEFFLER'S SYNDROME, PULMONARY EOSINOPHILIA

Transitory infiltration of the lung with eosinophilic cells is believed to be the result of the reaction of lung tissue after exposure to any one of a variety of antigens against which the lung was previously sensitized. The reaction can be induced experimentally in animals by sensitizing them to egg white, for example, and injecting the same antigen intratracheally after the proper time interval. In man eosinophilic reaction and infiltration occur in other tissues of the body in allergic states and it is surprising that involvement of the lung was unrecognized until it was described in 1932 by Loeffler. Transient pulmonary eosinophilia and eosinophilia of the blood occurs at times during allergic rhinitis, urticaria and asthma. Similar reactions are noted in some patients with amebiasis, ascariasis, trichiniasis, schistosomiasis, ancylostomiasis, cutaneous helminthiasis and other parasitic infections. They are not to be confused with the pulmonary reaction incident to the passage of some of these parasites through the lung during a stage in their life cycle as described on page 175. Eosinophilic pulmonary reaction with or without eosinophilia in the blood occurs at time during tuberculosis, brucellosis, coccidioidomycosis and probably in other chronic infections and has occurred during sulfonamide therapy. In many cases the cause is unknown. The pulmonary lesion is similar to that found in polyarteritis (periarteritis nodosa) and as described later in tropical eosinophilia.

Pathology

Little is known of the pathologic changes because the disease seldom is fatal. A patient who had had asthma for 7 years and died in an acute attack of allergic pneumonia was studied at necropsy.[1] The lungs showed advanced organization and a widespread alveolar and bronchial exudate, a predominance of eosinophilic cells and scattered patches of granulomatous inflammation. There were

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BAGASSOSIS

Bagasse disease of the lungs occurs in persons who inhale the dust of bagasse, the dry fiber of sugar cane after it has been processed Disease begins after 3 weeks to 2 years of exposure Characteristically, in the cases reported the onset was sudden and illness rapidly became severe enough to oblige rest in bed[1] There is dyspnea and cough with scanty mucoid sputum, occasionally blood tinged or bloody Fever, chills and sweating may be present Tachycardia and tachypnea are prominent Cyanosis may occur Considerable weight may be lost and weakness is protracted The course generally is variable and lasts from several days to several months Recovery is the rule if further inhalation of bagasse is avoided

Physical examination reveals only the signs of congestion in patches in one or both lungs, but a greater degree of involvement is found by roentgenography The shadows are those *of miliary diffuse areas radiating from the hilums* The apexes seldom are affected Low leukocytosis and in cases of long duration, polycythemia are noted

In lesions studied at necropsy, spicules presumably of bagasse, a fibroblastic reaction of the interstitial tissue, and alveolar cells with foamy cytoplasm were present in the alveolar spaces

Treatment is symptomatic Further exposure to bagasse dust should be avoided

BYSSINOSIS

Byssinosis is a rare condition affecting those who inhale the dust of low grade cotton It is uncertain whether the cotton itself or certain bacteria present thereon are the cause Like the so called *mill fever, Monday fever, heckling disease, grain or hemp fever* which are caused by the inhalation of dusts, it is a disease of the respiratory tract occasionally involving the lungs[2] The onset is sudden sometimes after a few hours or days of exposure There occur dry throat, arthralgia, aching fatigue, headache, cough, chills, fever, nausea, vomiting and conjunctival irritation The acute phase lasts only a day or two Prevention is of more importance than treatment Those who are affected should no longer be exposed to the dust which causes their trouble Working quarters should be ventilated or other provisions made to reduce the amount of dust in the air[3]

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CHEMICAL PNEUMONIA

Chemical pneumonia is the term applied to acute pulmonary lesions caused by the inhalation of air containing irritating substances or gases *Chemical pneumonia usually* is encountered as an occupational accident or in gas warfare[1] A form of chemical pneumonia occurs in persons trapped in burning *buildings* who inhale *noxious smoke* containing a variety of unknown irritants A comprehensive study of such injuries to the respiratory tract was made after a holocaust in Boston in 1942[2] A similar form of pulmonary irritation is described as silo filler's disease, caused by inhaling nitrogen dioxide Gases and vapors of chlorine, bromine, nitrogen oxides, fluorides sulfur oxides, ammonia hydrogen sulfide, phosgene and gases used in warfare are the chief causes[3] *The vapors of many solvents* are irritating to the lung tissue, especially certain acetates and formates, trichlorethane,

tetrachlorethane and other chlorinated hydrocarbons[4] Finely particulate matter suspended in air in the form of dust or smoke may cause irritation of the lungs *Cadmium* is of especial importance *Manganese* dust causes a severe form of pneumonia *Beryllium* dust may cause an acute pneumonia and long exposure to its results in chronic granulomatous lesions in the lung and elsewhere[5]

Pulmonary symptoms may be prominent in *metal fume fever* This disorder is caused by the inhalation of oxides of zinc copper magnesium and other metals It is attributed not to a direct effect of these oxides but to the absorption of denatured protein derived from the injured cells of the respiratory tract The disease is acute beginning after a latent period of a few hours The symptoms are dryness of the throat cough general aching fatigue chills fever nausea and sometimes vomiting After a few hours the patient sweats profusely and the temperature decreases The symptoms seldom last longer than 24 hours and pass off without after effects Leukocytosis occurs

Symptoms

In general pulmonary irritants also injure the mucous membrane of the upper respiratory tract the conjunctivas and occasionally the gastrointestinal tract The effect of any irritant on the lungs depends upon its concentration in the air on the duration of exposure or repeated exposure to it and on the condition of the patient There may be acute inflammation of the membrane of the respiratory tract immediately after the inhalation of irritants with choking and coughing In the early stages the patient may not show dyspnea or cyanosis but slight exertion may cause death from asphyxia Cyanosis may develop However even then relatively moderate signs of asphyxia and the absence of severe pain lead frequently to underestimation of the seriousness of the patient's condition There may be a period of deceptive well being for several hours or a day before shock pulmonary edema and collapse occur or the symptoms and signs of pneumonia appear Shock and poisoning may cause death in a few hours

Although the initial lesions are sterile secondary infection develops frequently caused by organisms present in the upper respiratory tract The symptoms and signs then resemble those of secondary bacterial pneumonia Death may occur before there is bacterial invasion Exposure to an irritant sufficient only to affect the upper respiratory tract may result in a tracheitis bronchitis or secondary bacterial pneumonia

Pathology

When an irritant in sufficiently high concentration is inhaled it causes a diffuse collection of polymorphonuclear cells edema necrosis desquamation of the alveolar cells and areas of acute inflammation around bronchi bronchioles and blood vessels Later infiltration with lymphocytic cells and proliferation of the interstitial tissue occur Bacterial invasion and pneumonia or abscess and subsequently chronic fibrosis bronchiectasis or emphysema may follow

In severe cases pulmonary edema may occur or the intercellular and alveolar spaces may be filled with coagulated fluid as a sterile hemorrhagic pneumonia The location of edema does not depend so much on gravity and posture as edema of other origin Inflammatory changes are not evenly distributed in the lungs and areas of atelectasis and emphysema are present

Treatment

The treatment of the early stages of chemical pneumonia is essentially the same as for shock and circulatory collapse The symptomatic treatment is the same as that outlined on page 150 The value of prophylactic administration of antimicrobic agents to prevent bacterial invasion is not established Cortisone is said to be beneficial in the treatment of beryllium pneumonia A thorough appraisal of the methods used to combat the respiratory tract injuries incident to inhaling smoke in a holocaust is available[2] All the methods of treatment were far from satisfactory and the results were discouraging Aminophyllin atropine adrenalin caffeine and coramine were of no value Expectorant drugs were of questionable value The importance of keeping the respiratory tract moist and open by

simple means was emphasized Application of bland oils to the nose and pharynx humidification of inspired air and administration of oxygen were important Tracheotomy was used if all other measures failed Opiates were most useful in relieving pain Antimicrobic therapy seem to control pulmonary infections in many instances If secondary bacterial pneumonia occurs, its treatment is the same as that outlined on page 150

BERYLLIUM PNEUMONIA

Van Ordstrand reported 12 deaths among 98 victims of beryllium pneumonia[7] After exposure to fumes and dusts of beryllium salts or alloys, the disease begins insidiously or suddenly and resembles an ordinary infection of the respiratory tract There is a relatively nonproductive cough low fever and often hyperglobulinemia Roentgenographic shadows appear in the lungs in 2 or 3 weeks Illness in the acute form lasts a few weeks to several months Death in severe cases occurs after 2 or 3 weeks from asphyxia with or without cor pulmonale Recovery may be complete with no residual pulmonary changes Histologically fresh lesions have an intra alveolar edematous exudate, and in contrast with chemical pneumonia from other causes mononuclear cells predominate in granulomatous areas

The chronic form may be delayed for months to as long as 10 years after termination of exposure It appears to be a systemic disease with primary or incidental pulmonary involvement The symptoms and signs are those of a debilitating disease Fine disseminated nodular infiltrations are seen roentgenographically Pathologically there are sarcoid like, interstitial, granulomatous changes In therapy, corticotrophin and cortisone are the drugs of choice They have been shown to cause striking if temporary improvement in a number of patients

SILO FILLER'S DISEASE

The inhalation of fumes in or near freshly filled silos may cause mild to fatal disease[8] The irritating gases are nitrogen dioxide and nitrogen tetroxide Symptoms begin a few hours to several days after exposure There are cough and dyspnea, a choking sensation and weakness After a variable time, these symptoms abate and after 2 or 3 weeks a second phase occurs, often with chills, fever, cough, dyspnea and cyanosis Many fine rales appear in both lungs with evidence of bronchiolar obstruction Roentgenography reveals uniform infiltration generally with discrete nodular densities Leukocytosis and retention of CO_2 occurs Recovery may be complete, or chronic illness with obliterative bronchiolitis or death may result

Prevention

Persons should avoid entering freshly filled silos for 7 to 10 days Silos should be ventilated, especially at their base

Treatment

There is no specific treatment Steroid hormone therapy may be helpful

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PULMONARY CHANGES DURING UREMIA "UREMIC PNEUMONIA"

Among 107 patients with uremia studied at necropsy 66 had pulmonary involvement.[1] Of these 38 had coexisting bacterial pneumonia or infarcts. The rest were lesions regarded as uremic pneumonia. There was no significant relationship between the duration of the uremia and the onset of pneumonia. During life it usually is impossible to distinguish the lesion from other pulmonary diseases. Other observers reject the concept of uremic pneumonia and believe the lesion to be caused by pulmonary congestion and edema from cardiac failure with or without secondary infection.

Grossly the involved area, chiefly in the hilar regions, was rubbery, hyperemic and edematous, especially if there was cardiac failure. Fibrinous pleuritis often was present. The alveoli contained a network or dense masses of fibrin with erythrocytes and macrophages. Granulocytes were present if there was bacterial infection. Involvement of the interstitial tissue and bronchiolitis were not prominent. Necrotizing arteritis was observed by some investigators[2] and not by others.[1] Plugs of debris in the finer air passages account for the dyspnea and cyanosis which occur. In long standing disease there are obliterative and fibrotic changes. The lesions resemble those of rheumatic, radiation, chemical, resolving or organizing pneumonia.

Clinically the symptoms and signs differ from those of pulmonary edema. There are mild or severe dyspnea and cyanosis. Cough and hemoptysis occur, but fever is not prominent. The heart usually is enlarged. The physical signs are minimal, but roentgenography may reveal surprisingly extensive shadows. Uremic pneumonia may be detected first by roentgenography. The dense symmetric shadows are confined to the inner lung fields and the periphery and bases often are clear. They are micronodular and floccular and resemble those seen in pulmonary edema, sarcoidosis, pneumoconiosis, and in rheumatic or viral pneumonia, but they differ from those of cardiac failure, miliary tuberculosis and tumors.[3]

The presence of uremic pneumonia is ominous. Most patients die. In those who recover the pulmonary changes disappear as the uremia and cardiac failure improve. Treatment consists of administration of oxygen under pressure and the correction of cardiac failure and the cause of the uremia.

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PULMONARY INVOLVEMENT IN SARCOIDOSIS

It is uncertain whether sarcoidosis is an entity; it probably is caused by a number of agents. It usually is a chronic disease during which the lungs are involved at some time during its course in over 90% of victims. Both lungs usually are affected with bihilar lymphadenopathy and a variety of lesions including a reticular distribution, miliary dissemination, small or large nodules and diffuse lobar involvement.[1,2]

There is no correlation between the extent of pulmonary infiltration with sarcoidal lesions elsewhere or with the respiratory symptoms. There may be no symptoms, or mild cough, or severe progressive dyspnea caused by destruction of tissue, fibrosis or cor pulmonale. Roentgen evidence is uncharacteristic as indicated in the first paragraph. Lesions may regress and leave no trace or may increase and cause death by asphyxia or fibrosis. Emphysema and bronchiectasis may develop. Concurrent tuberculosis is present in over 10% of cases.

Diagnosis is made by the nature of the general disease, by biopsy and roentgenography. Cases have been confused with histoplasmosis and other mycotic infections, neoplasm and other granulomas.

Adrenocorticotropic hormones have been used therapeutically in some cases with temporary success.

WEGNER'S GRANULOMATOSIS

This rare condition may be confused with polyarteritis and sarcoidosis It was called foam cell pneumonia by Churg and cholesterol pneumonitis by others It is a syndrome characterized by necrotizing granulomatous lesions of the respiratory tract generalized arteritis and focal glomerulitis Clinically there are symptoms of sinusitis and pulmonary inflammation and variable evidence of systemic arteritis The duration is about 6 months and all recognized cases have been fatal The cause is unknown and treatment is unsatisfactory [3]

ALVEOLAR PROTEINOSIS

Alveolar proteinosis has been newly described as a chronic condition of unknown cause Since the first 27 cases was observed for only 5 years the course of the disease is not known fully It may begin gradually with pneumonic symptoms There are slowly progressive dyspnea cough sputum malaise and loss of weight Roentgenographically fine diffuse feathery or vaguely nodular soft densities resemble those of pulmonary edema The shadows diminished in intensity in 5 patients but remained unchanged in 13 Eight patients died Biopsy specimens revealed yellowish gray nodules containing pus like substance At necropsy large areas of confluent consolidation were present [4]

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Med 258 1123 1958

PULMONARY INVOLVEMENT IN DISEASES OF THE COLLAGEN SYSTEM

In the last decade or two much attention was given to a variety of diseases presumably of allergic origin in which involvement of collagenous tissue is prominent These apparently are caused by hypersensitive reactions to proteins or chemicals and occur as polyarteritis (periarteritis nodosa) lupus erythematosus disseminatus dermatomyositis and scleroderma Although these widely different and variable diseases seem to have little in common many observers incriminate a common etiologic factor namely allergy because of a similar reactive cellular mechanism operative in each It is probable however that there are other causes as well

Pulmonary lesions regarded as pneumonia occur at times in each and are similar [1,2] Bacteria free pneumonia may occur in varying degrees of severity and extent only once in the course of the disease or in acute or indolent episodes during chronic disease and often is found at necropsy Secondary bacterial invasion may occur The signs symptoms and roentgenographic shadows are uncharacteristic and variable ranging from those of congestion to consolidation They may resemble those of allergic pneumonia Microscopically there are infiltrations of the alveolar walls septums and interstitial tissue with monocytes and red cells hemosiderin laden macrophages edema and the formation of alveolar hyaline membranes Eosinophilic cells may or may not be present After prolonged pulmonary involvement especially in scleroderma cysts dense fibroblastic and collagenic scar formation develop Because of the presumed nature of this group of diseases corticotrophin and cortisone may be helpful in therapy

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CHAPTER 8

Tuberculosis

J Arthur Myers, M D

Acid Fast Bacilli

When Koch announced the discovery of the tubercle bacillus (1882) there was thought to be only one type However Maffucci reported having isolated the avian type in 1889 and Smith the bovine type in 1898 Bacteriologists have since found a number of acid fast bacilli which appear essentially the same on microscopic inspection but have other characteristics by which they can be readily identified Some of them cause tuberculosis in man and animals while others are non pathogenic, as shown in the following classification

GENUS MYCOBACTERIUM

Pathogenic Acid Fast Bacilli
- Mycobacterium tuberculosis
  - Human type—frequently causes disease in man and also occurs in animals such as swine and parrots
  - Bovine type—causes most of the tuberculosis in cattle frequently attacks humans and many domestic animals
  - Avian type—causes tuberculosis in fowls It also attacks swine, sheep horses, and occasionally humans
  - Cold blooded type—causes disease in fish frogs snakes and turtles
- Mycobacterium paratuberculosis (Causes paratuberculosis Johne s disease in cattle)
- Mycobacterium leprae (Causes leprosy)

Saprophytic Acid fast Bacilli
- Mycobacterium smegmatis
- Mycobacterium phlei (timothy hay bacillus)
- Mycobacterium stercoris (most bacillus found in cow manure)
- Mycobacterium butyricum (found in butter)

GENUS MYCOLEANA

Acid fast bacilli used

Where or when the tubercle bacillus first appeared in the world is unknown Ravenel says "It is certain that the various types of tubercle bacillus known to us have sprung from a stock common to them all and that they have acquired their racial peculiarities by residence in different animals through which they are subjected to a difference in food temperature and resistance In other words the struggle for life is carried on in the various species of animals under varying conditions the results being that in each animal the tubercle bacillus acquired properties which best enable it to carry on life in that particular host"

Just as tubercle bacilli long ago adapted to certain situations they apparently have continued to change Dubos *et al* say "As far as is known all the strains of BCG presently in use are derived from the attenuated culture first obtained by Calmette and Guerin Although there is as yet no incontroverted evidence that this culture has ever recovered full virulence, there is no doubt that it has undergone considerable variations in the course of its long career Indeed it would be very surprising if it had not K A Jensen for example has pointed out that the strains available in Scandinavia at the end of World War II varied appreciably with reference to the severity of the skin lesions which they could elicit in normal guinea pigs Similarly it has been observed in our laboratory that three strains of BCG obtained from American collections differ significantly in their ability to produce pulmonary lesions in mice following intravenous injection

Wood *et al.* described disease in 17 persons infected with a *chromogenic acid fast bacillus* designated "yellow bacillus," in five of whom it was fatal. The only definite differential diagnostic procedure was by bacteriological study and animal inoculation. The "yellow bacillus" usually failed to produce progressive fatal disease in guinea pigs but regularly killed hamsters. Chromogenic acid fast bacilli, some of which were pathogenic and others proved to be saprophytes, have been reported by others.

In recent years *atypical* tubercle bacilli have been isolated and grouped by a number of authors including Runyon and Keltz, Colton and Lester. Keltz et al. says "The ultimate basis for judging a culture to be atypical was made upon a careful inspection of colonial morphology. It was immediately apparent that the 164 atypical strains isolated from our patients fell in three groups which generally conformed to those described by the Cooperative Study of Mycobacteria. For purposes of clarity the three groups may be differentiated as follows:

Group I—Photochromogenic strains. These form a lemon yellow pigment during growth if exposed to light. This group comprised 22.6 per cent of our atypical cultures isolated from patients.

Group II—Non photochromic strain. These are white, beige, or buff to yellowish, the pigmentation, if any, is not light conditioned. This group comprised 2.4 per cent of the atypical cultures isolated.

Group *III*—Deeply chromogenic yellow-orange strains which are pigmented even in complete darkness (skotochromogenic). This group comprised 75 per cent of the atypical cultures isolated.

It appears, therefore, that numerous changes may now be occurring among tubercle bacilli caused by antituberculosis drugs. If resistant mutants tend to predominate, drug treatment of tuberculosis may become complicated.

There are probably only few places in the world where tubercle bacilli do not exist today. They are found in the immediate environment of persons and animals who have contagious tuberculosis. It is only when they lodge on or find entrance to objects or substances such as food or clothing that they may be carried away from the patient's immediate environment. *Thus the tubercle bacillus is not ubiquitous as was at one time believed.*

Tubercle bacilli are usually eliminated from humans in sputum and feces from lesions in the lungs. If tuberculosis exists in bones, joints, pleura, or superficial lymph nodes, sinus tracts may communicate with the surface of the body through which tubercle bacilli are discharged. When clinical lesions are present in the kidneys or other parts of the genito urinary tract, bacilli may be eliminated in abundance in the urine. Whenever these organisms reach the outside world they are of danger to persons and some animals who come in contact with them.

Tubercle bacilli do not multiply outside the bodies of persons and animals except under laboratory conditions; however, they may remain alive and virulent for four months in dark, cool places. When sputum containing tubercle bacilli is spread thinly on glass and exposed to direct sunlight in summer, the bacilli are destroyed in 10 minutes, but on clothing it may require 24 to 30 hours.

Heat is not well tolerated by tubercle bacilli. When dry at 100°C. they live for about 20 minutes. However, in the presence of moisture 95°C. destroys them in 1 minute, 70° in 10 minutes and 60° in 1 hour. Alcohol quickly destroys them. For wet surfaces 95%, for dry 50% and for wet or dry 70% is best. Carbolic acid in 5% solution destroys them in a few minutes.

Tuberculosis is *rarely congenital*. Therefore, in nearly all persons who become infected, bacilli reach their bodies after birth. The two main *portals of entry* to the human body are the *digestive tract* and the *respiratory tract*. One school clings to the view that most persons are infected by inhaling bacilli, the other by ingesting them. In reality it makes little difference since their focalization may be the same in either case. Ravenel says: "It is fallacious and misleading to claim that food tuberculosis should show itself in a primary intestinal lesion." Schroeder pointed out that no one can reasonably doubt that swallowed tubercle bacilli will shortly reach the lungs since they pass through the healthy wall of the

intestine into the thoracic duct three hours after they enter the stomach. He also called attention to the fact that it is a simple matter to produce tuberculosis in the lungs by introducing tubercle bacilli into the digestive tract which he and co-workers had proved. Calmette and Guerin came to the conclusion that in the normal condition of natural infection the digestive canal is the principle door of entrance of tubercle bacilli.

The *eye* is also a portal of entry, particularly in infants and young children.

In women the *genital tract* may serve as a portal of entry but probably only in the event tuberculosis exists in such organs of men as the prostrate gland.

Normal skin is resistant and probably never admits tubercle bacilli, however, slight abrasions make it extremely vulnerable. Numerous cases are on record of lesions developing on the hands following injury while doing postmortem examinations.

With the discovery of the tubercle bacillus accurate diagnosis of tuberculosis during life was made possible for the first time in history. These organisms were found in various secretions and excretions of some persons and animals. It was assumed that they would be found in this manner in everyone who had tuberculosis, therefore, if they were not detected the individual was thought to be suffering from some other condition. However, it was later learned that when tubercle bacilli are found in *sputum* the areas of disease in the lungs have often attained an advanced stage. Thus accurate diagnosis is made in this manner after the disease has become contagious.

When it was known that pulmonary tuberculosis usually passes through a long period of evolution before there is sputum to examine, the idea was conceived of examining *stomach washings* whenever a demonstrable lesion in the lungs is suspected of being tuberculous on the ground that a small amount of material which might be eliminated from the region of the lesion would pass through the bronchi and trachea and be swallowed after reaching the pharynx. De Abreu presented a technique for doing pulmonary washings in search of tubercle bacilli. He recommends this for persons who have lesions but do not have sputum or when bacilli have not been found by the usual methods.

When one considers that in the examination of sputum, gastric washings, pleural fluid, etc., by the direct smear method, an extremely small amount is inspected under the microscope and that some entire specimens collected from the same individual may contain tubercle bacilli while others do not, it is only to be expected that the organisms may not be seen in all specimens. Sweany states that approximately 1,000 and others believe that from 10,000 to 100,000 tubercle bacilli must be present per cubic centimeter of sputum before they are found on direct smear. Therefore, refined methods have been devised for identifying tubercle bacilli including planting suspected material on culture medium and introducing it into laboratory animals.

Occasionally one is at a loss to determine the etiological diagnosis and biopsy is necessary. This may be true in cases of suspected superficial lymph node tuberculosis, tracheo-bronchial lesions, those of the bones, joints, pleura and even some pulmonary lesions.

PRIMARY (FIRST INFECTION TYPE) TUBERCULOSIS

Tuberculosis is not *inherited*. It may be *congenital* if the disease involves the placenta. From the number of cases reported in the literature it appears that congenital tuberculosis occurs so rarely as to be of little significance.

Most of the cases of first infection type of tuberculosis are the result of *postnatal infections* by either the human or bovine type of tubercle bacillus.

PATHOGENESIS

When tubercle bacilli enter the human body, regardless of age, they are phagocytosed by neutrophils some of which enter the blood and lymph streams resulting in bacteremia.

The numerous tubercle bacillus-bearing neutrophils circulating in the blood and lymph streams quickly lodge in various locations

including kidneys spleen bones joints and lungs More are deposited in the lungs than elsewhere Relatively few organisms are focalized in one place in each of which tubercle formation is likely to occur This is of marked advantage to the defense elements including monocytes lymphocytes and fibroblasts in that they can cope more successfully with relatively few in each of many places than a large number in one area Apparently this accounts in *part for the almost uniform benignity of primary tuberculosis per se The defense mechanism encountering relatively small numbers in* any given place is able to surround them effectively before sensitivity to tuberculoprotein is well established and the subsequent more permanent encapsulation proceeds without interruption

From these points of focalization some tubercle bacilli usually find their way through lymphatic channels to regional lymph nodes *Many are retained by these nodes where tubercle formation occurs similar to that at the* first sites of focalization The areas where tubercle formation is occuring are tuberculous lesions (lesion is defined as "an alteration of structure or of functional capacity due to injury or disease") In fact these lesions begin to form immediately after tubercle bacilli are *focalized The lesion at an original site together with those which develop in regional lymph nodes constitute a primary tuberculosis complex* Obviously these complexes are multiple as they are likely to develop at various points where the original focalizations of tubercle bacilli occur Lesions of these complexes become surrounded by fibrous tissue and in many calcium and bony encasements develop around them

As primary tuberculosis complexes develop the body tissues including the skin become grossly sensitized to the protein of tubercle bacilli within a few weeks after the initial invasion occurs

If an overwhelming number of tubercle bacilli participate in the initial invasion the defense elements may not be able to cope adequately at all of the points of focalization Thus when allergy appears tuberculoprotein liberated from foci not well encapsulated may *immediately* produce reinfection type of tuberculosis

INCIDENCE

*It was formerly believed that nearly all children develop the first infection type of tu*berculosis before reaching adulthood It was then called the childhood type In 1900 Naegeli found gross or microscopic evidence of tuberculous infection in 98% of adult bodies which were subjected to postmortem examination This situation still obtains in some parts of the world In this country, however as the disease among cattle was brought under control and large numbers of persons with con*tagious tuberculosis were isolated in hospitals* and sanatoriums the incidence of the first infection type of tuberculosis among children and young adults was markedly reduced Indeed in some places in this country the annual attack rate is already less than 33% Thus if the present attack rate continues it is obvious that by the time children reach the age of 15 years less than 5% *will have the first infection type of tuberculosis* and when they are 60 years old less than 20% will have had this type of disease

Inasmuch as the span of life is approximately seventy years obviously, *far more tuberculosis of the first infection type develops among adults than among children* and more than 80% of the present children will be able to live *out the span of life without infection with tu*bercle bacilli There is evidence moreover that the infection attack rate is decreasing in these areas and thus should result in even much lower incidence of first infection type of tuberculosis in the next generation

DIAGNOSIS

Tuberculin Test

With the introduction of *tuberculin* there became available a *method of determining* accurately the presence of this type of disease in the living body Ghon demonstrated that whenever individuals reacted to tuberculin even though there was no evidence of clinical tuberculosis he could find tuberculous lesions

in their bodies on postmortem examination He dissected in detail the lungs and other organs of 184 bodies "Only in this way," he states "was I able to detect slight tuberculous lesions in some cases where there had been positive tuberculin reaction" Because of their small size the detection of some of the pulmonary foci was "a very difficult task and often required considerable time" Again he says "The smallest foci were scarcely found at all in the cases with anatomical healing This fact is of importance it explains to us why it is often difficult to find such foci " In five of his cases the foci were located only in exthrathoracic organs

With Ghon's findings which have been confirmed on numerous occasions in both man and animals (veterinarians have done postmortem examinations on 4 077 995 cattle slaughtered because they reacted to tuberculin) it became obvious that *everyone who reacts characteristically to tuberculin has tuberculosis* This fact relegated to the discard the idea that there is a sharp dividing line between tuberculous infection and tuberculous disease

Inasmuch as the tissues become allergic to tuberculo-protein during the formation of primary tuberculosis complexes and remain so as long as tubercle bacilli are alive and inasmuch as this sensitivity can be detected with a high degree of accuracy by the proper administration of tuberculoprotein *the tuberculin reaction is definitely diagnostic of the presence of the first infection type of tuberculosis* hence various phases of the tuberculin test are deserving of discussion

The first testing substance was presented by Koch in 1890 and was known as "Koch's lymph" but soon it was given the name "tuberculin" It contained no tubercle bacilli either alive or dead as the processing provided for the destruction of these organisms by heat and their removal by filtration after which phenol was added in a concentration that made germ life impossible This is now referred to as OT (original tuberculin)

The protein of the tubercle bacillus is the active principle in producing the tuberculin reaction The idea was then conceived of using only tuberculoprotein as a testing material Long and Seibert are responsible for such a preparation now available under the name *Purified Protein Derivative* (PPD)

Tuberculin made from either the bovine or the human type of tubercle bacilli is satisfactory in testing for both the bovine and the human types of tuberculosis In this country tuberculin is nearly always made from the human type and is used in testing of humans as well as animals In testing for infection with the avian type of tubercle bacilli it is best that tuberculin be made from this type of organism

Prior to 1907 the tuberculin test was administered by *the subcutaneous method* The reaction was determined largely by the development of symptoms such as fever which appeared within 24 hours after administration The amount of tuberculin used in this test was so large that it often harmed sensitized persons

Clement Pirquet Vienna introduced a test (1907) which consisted of making a small superficial abrasion of the skin to which tuberculin was applied If tuberculosis was present in 48 to 72 hours a reaction consisting of local induration and redness appeared This proved to be a useful test and was entirely harmless Simultaneously but independently Calmette Paris and Wolff Eisner Berlin (1907) developed the *ophthalmic* test which consists of introducing a drop of 1 per cent solution of tuberculin between the eyelids If the individual reacted within 24 to 48 hours there was swelling and redness of the conjunctiva and adjacent parts and exudate accumulated in the conjunctival sac While the test was accurate keratitis and even ulceration of the cornea often developed therefore this method was abandoned

Lautier France (1908) administered tuberculin by moistening a *pledget of absorbent cotton* with a 1 per cent solution This was applied to the skin and covered with rubber tissue protected with cotton and a bandage and left in place for forty-eight hours This was later refined by Vollmer and Goldberger and is now known as the *patch test*

Mantoux France (1908) presented a method which consists of introducing into the layers of the skin with a hypodermic syringe a dilu



Fig 1 Forearms of two girls who had 0 1 mg of tubercul n administered intracutaneously The upper shows no
the site of adm
bacilli are prese
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tion of tuberculin of known strength This is the *intradermal* or *intracutaneous test* of Mantoux In 48 to 72 hours a reaction is manifested by induration or edema usually surrounded by an area of hyperemia at the site of administration Advantages of this method are that a measured amount of tuberculin is introduced and can not be removed by the subject No tape or bandaging is necessary and the test can be administered in a short time The same year Moussu *Alfort France* used this method to test cattle This is now considered the most accurate method of administering tuberculin

The inner surface of the forearm is convenient and is the usual site of administration (Fig 1) Other parts of the body are equally *satisfactory as far as the reaction is concerned* Some prefer the interscapular region and others the inner surface of the thigh For more than 35 years in testing adults we have administered tuberculin over the deltoid muscle immediately below the shoulder joint This is a convenient site and if reaction occurs it is obscured from view by clothing However it has no advantage from the standpoint of reaction

One experienced physician or nurse can administer tuberculin by the intracutaneous method to from 300 to 500 persons per hour *Individual syringes should be used for such* substances as coccid o din histoplasmin and tuberculin unless the syringes are soaked in dichromate cleaning solution after each use If this is not done the active principles of these various substances may be absorbed by the glass so as to cause inaccuracy and confusion in the specificity of the various tests

The usual procedure consists of administering intracutaneously 0 1 mg of original tuber

culin (OT) or 0.00002 mg. of PPD as the initial dose. Seventy two to ninety six hours later, nonreactors receive 1.0 mg. of original tuberculin or 0.005 mg. of PPD. A single test dose consisting of 0.0001 mg. PPD is being extensively studied by Palmer. This dose equals 5 international tuberculin units (5TU).

Tests should be read 72 to 96 hours after administration. An area of induration and/or edema at the site of administration of 5 to 10 mm. in diameter is classified as one plus (+); from 10 to 20 mm. two plus (++); above 20 mm. three plus (+++). With marked induration and *necrosis* the reaction is classified as four plus (++++). An area of induration less than 5 mm. in diameter is best recorded as a questionable reaction.

Degree of reaction does not indicate extent of disease; therefore many physicians prefer to record only that the individual is a reactor or a nonreactor to tuberculin.

The tuberculin test fails to reveal presence of tubercle bacilli for the first 3 to 7 weeks after their initial invasion. This period, known as the pre allergic stage, is required for sensitization of tissues to develop so as to cause a characteristic reaction. The usual test dose fails occasionally in persons overwhelmed by acute tuberculosis and those approaching death from chronic disease. During acute non tuberculous infections, allergy may be depressed. However, in none of the above situations is sensitivity completely lost. It can be elicited by larger doses of tuberculin.

Cases have been reported with all diagnostic evidence of pulmonary tuberculosis including *cavitation and acid fast bacilli in the sputum* but no reaction to tuberculin. However, bacteriological studies have sometimes revealed that the organisms were not tubercle bacilli. This has also been observed in persons whose disease is caused by chromatogenic acid fast bacilli.

In tuberculous lesions of both primary and reinfection types of long standing with no reinfection, sensitivity of the tissues wanes and often reaches a level at which the usual first dose is not sufficient to evoke a reaction. This may also be true of an intermediate dose. Usually enough sensitivity remains to be elicited by a reaction to the second dose. Occasionally even this is not sufficient, particularly among elderly persons.

Austrian (1927) reported the loss of sensitivity to tuberculin in several cases. Paretzky (1936) called attention to disappearance of skin sensitivity in 80 cases. Dahlstrom (1940) examined the dispensary records of the Henry Phipps Institute of 3,919 members of 513 families under observation from 5 to 15 years. Only 0.4% of 1,090 people giving a three plus reaction to the standard first dose of tuberculin became non reactors, but 70% of 185 persons with only one plus reaction to the second dose later failed to react.

It has been generally believed that the individual who reacts to tuberculin will always be a reactor. *However, it now appears that in the bodies of some persons all tubercle bacilli die and the tissues lose their sensitivity to tuberculin.* A considerable number of children and young adults with characteristic tuberculin reactions soon after exposure to contagious cases have been observed to revert within a few months, suggesting that tubercle bacilli had disappeared. How frequently this occurs or how long an interval is required has not been determined. Therefore the individual who reacts to tuberculin should be retested periodically. There are persons who do not react to the first dose but present a reaction to the second. Palmer *et al.* are of the opinion that these are nonspecific reactions. Some of them may be caused by acid fast bacilli other than *mammalian types.* Objection has been offered to the term "nonspecific" by those who feel that it must be a specific reaction for tuber*culoprotein of some forms of acid fast bacilli*, even those that may not be pathogenic for man. Infections with avian type of tubercle bacilli do not always result in characteristic reactions when tuberculin made from mammalian types is employed. It has also been stated that there has not been sufficient documentation to justify the term nonspecific, inasmuch as allergy from natural infection with human and bovine types of tubercle bacilli varies considerably from time to time in the same individual. It evolves slowly during the first few weeks after infection, reaches a plateau which it may maintain for months or years and may later slowly wane. Before this plateau is



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reached and after allergy begins to wane, the usual second dose of tuberculin is often required and later even larger doses may be necessary to elicit its presence. Moreover, cases are on record who reacted only to the second dose of tuberculin but lesions in resected units of their lungs or those found at postmortem contained unmistakable pathogenic organisms.

A similar problem was recognized by veterinarians in the nationwide tuberculosis eradication program in cattle. Although attention was called to this situation in 1913 by Perard and Ramon (France), Traum apparently for the first time in the United States observed tuberculin reactors among cattle in which tuberculous lesions were not observed at autopsy. Subcutaneous swellings or nodules tubercle-like in character were sometimes present, usually on the lower parts of the extremities. Crawford pointed out that these were later found to contain acid-fast organisms which were identified as soil bacilli.

Persons who do not react to tuberculin should be tested at least annually. The belief that only children should be tested with tuberculin is obsolete. There is no age at which tuberculin testing is not of value. The test should be administered to all persons from infancy through senility.

Original Tuberculin (OT) and Purified Protein Derivative (PPD) as they are administered today *do not sensitize the tissues*; therefore, repeated tests will not result in reactions in persons who do not have tubercle bacilli in their bodies. Most of the former apparent discrepancies which caused criticisms of the tuberculin test have been satisfactorily explained. They were due to such factors as use of poor testing material, improper administration of the test, inadequate dosage, inability to interpret the test, misinterpretation of some other phase of the examination such as x-ray inspection, and finding that recovered acid-fast bacilli were not tubercle bacilli. When a reaction is present, it informs one that the body contains living tubercle bacilli and, therefore, first infection type of tuberculosis is present. *There is no test in medicine that has been so extensively employed and the results so carefully checked by postmortem and biopsy examination as the tuberculin test.* Among animals it has been used throughout the world since 1892. From 1917 to 1958 in the United States alone, 396 687 286 tests were administered to cattle and 4 077 995 reactors were slaughtered and examined postmortem.

The term "nonspecific tuberculin reactor" among animals and people has been used freely but without as much evidence to justify its use as many workers desire. For a long time the term "no lesion reactor" was applied to cattle which reacted to tuberculin but in which necropsy revealed no lesion. Attention was then called to the fact that such animals might well have lesions which were missed at necropsy. Therefore the term "no visible lesion reactor" was introduced. Such animals are now often referred to as nonspecific reactors. It is apparently well established that avian and human types of tubercle bacilli and possibly some saprophytes, especially soil bacilli, sometimes produce sensitivity of tissues as revealed when tested with mammalian tuberculin. However, when an animal reacts there is no way of being certain which type of organism is responsible except through recovery of bacilli from biopsy or postmortem material and determining its type.

Many workers object to the term "nonspecific tuberculin reactors" because the organisms have not been recovered and typed. Most likely this problem will not be solved until someone does meticulous postmortem examinations on the carcasses of a sufficient number of so-called nonspecific reactor cattle as Ghon did on human bodies between 1908 and 1912. None of the 184 persons whose bodies he examined had any evidence of tuberculosis during life except the tuberculin reaction. In some of them ordinary postmortem examination failed to reveal lesions. However, since he had set out to determine whether the tuberculin reaction always means the presence of lesions, in a number of cases he went back for a second and even a third look and found lesions in 183 of the bodies. The remaining one was not completely studied.

Sweany says, "The other drawback to antimicrobial therapy is due to that fundamental law of nature, the ability of living species to adapt to changing environment by the sur-

vival of mutants when changing environment threatens to exterminate the parent species Molecular rearrangement within the genes (genotypic changes) result in variations in the offspring that are better adapted to the new conditions the end product of the tubercle bacillus (as well as all other species of living organisms) is therefore the result of a rigid selection of mutants to fit environments in which they are obliged to grow"

Again Sweany says "In spite of the fact that the tubercle bacillus has appeared to be a rather stable parasite many variations have been observed since its discovery involving among other changes variations in morphology virulence chromogenesis and gross colony formation"

Size of the carcass of the bovine reactor makes the quality of postmortem work that Ghon did exceedingly time consuming However there is little likelihood that any other method will determine if and when the term non specific tuberculin reactor is justified Recently this belief was partially supported when in 1956 Nassel Germany reported pathological and bacteriological findings on 1000 tuberculin reacting cattle in which no tuberculous lesion was found at the usual post mortem inspection The infection was found in 50 2 per cent of which 86 6 per cent detailed gross examination revealed the lesions and 13 4 per cent culture or animal inoculation was necessary Of the lesions found 86 5 per cent were in the lungs 12 1 per cent in mesenteric lymph nodes and 1 4 per cent in the udder or its lymph node Thus one half of the problem of no visible lesion reactors was explained The bovine carcass is large and lesions may appear in areas remote from their usual sites therefore one wonders if the remainder of this problem would be largely solved by more extensive and intensive examination In any event until this is done the specificity and accuracy of the tuberculin test should not be questioned This term is also used in tuberculin testing among people where its justification will also have to await meticulous postmortem examinations of so called non specific reactors

Paterson points out that the tuberculin test has been so successful in detecting bovine tuberculosis as to almost completely eradicate this disease in several countries He says there comes a point in all eradication campaigns when the cattle population is nearly free from tuberculosis but a nucleus remains in which the ability to distinguish the true case of tuberculosis from the non specific reactor becomes increasingly difficult because of gaps in knowledge of known causes of non specific sensitization and lack of appreciation of unknown causes In this situation it is sound practice in individual herds to dispose of doubtful animals rather than risk their being a focus of infection No visible lesion reactors become more important with increasing freedom from tuberculosis as they form a persistent group which may harbor a case with minimal lesions

Rice Christiansen Lindau and others have called attention to the importance of periodically testing cattle herds with tuberculin even though the incidence of reactors is extremely low Indeed this is now regarded as an excellent tuberculosis case finding method among humans inasmuch as cattle are often found to have been infected by owners hired hands etc This applies especially to persons whose disease is caused by the bovine type of tubercle bacilli and therefore pass the organisms back to cattle Although human type of bacillus usually does not cause progressive disease in bovines it often does result in nodular lesions with sensitivity to tuberculin Therefore people who have infected cattle with human type of bacilli may have their disease found on investigation after animals have converted to tuberculin reactors

History of exposure to a contagious case of tuberculosis is not of great reliability since 50% or less of persons with tuberculosis know where or when they were infected Moreover the tuberculin reaction informs the physician that exposure has occurred

Symptoms

When allergy appears so it can be detected by the tuberculin test mild symptoms may be present or absent Wallgren studied carefully a group of children who had been exposed to tuberculosis but on first examination they did not react to tuberculin He



Fig 2 Roentgenogram taken December 1931 of chest of girl of 6 months tuberculin reactor Mother had contagious tuberculosis *Primary tuberculous infiltrate right base No symptom*

Fig 3 From roentgenogram taken November 1948 *of same chest as seen in Figure 2 Photo*fluorogram taken November 1950 reveals no change Note evidence of calcium deposits right lower lung field right hilum and right paratracheal region No evidence of clinical tuberculosis to date

observed them with great care and almost *simultaneously* with the appearance of fever they were found to be tuberculin reactors However not all of them had fever The febrile reactions were of short duration usually lasting not longer than ten days or two weeks The *temperature elevation in such cases* usually ranges between 99 and 101°F however in the occasional case it may reach 102 or 104°F During the febrile period other symptoms may closely simulate those of a cold or influenza When symptoms are present they may be so mild that they are ignored by the patient or his family If they are more severe and a physician is called he is likely to mistake them for the symptoms of other acute infections

Examination

A *tuberculin* reaction determines with uncanny accuracy the presence of primary tuberculosis however it affords no aid in locating lesions *Physical signs* are of almost no value in the detection of first infection type of tuberculosis in the lungs of children or adults However the conventional physical examinations should always be performed but the point which requires emphasis is that *when abnormal signs are not elicited one has not ruled out first infection type of tuberculosis* In a small percentage of persons soon after becoming sensitized to tuberculoprotein one or more areas of disease may be located in the lungs by the dense homogeneous shadows they cast on *x ray* films (Fig 2) These areas *of disease may be located in any part of a* lung from the apex to the base Various names have been used to designate them such as epituberculosis and primary tuberculous infiltrates When one first observes their *shadows one cannot differentiate them by* shadow alone from reinfection type of pulmonary tuberculosis pneumonia abscess etc

Wallgren says "This perifocal reaction as regarded histologically is not a typical tuberculous process of inflammation but consists of hyperemia with desquamation of alveolar cells lymphocytic infiltration and edema Here and there however occur minute necrotic foci and giant cells thus indicating the etiologic origin of the pneumonic process The same reaction is produced in the lymphatic glands which increase rapidly in size" The pneumonic area may persist for many months often more than a year and then slowly disappear leaving no trace that can be detected by x ray inspection However at some later time evidence of deposits

of calcium may be seen at the site of the previous shadow and in regional lymph nodes (Fig 3). These x ray findings are rarely seen in more than 5 to 8% of persons who have the first infection type of tuberculosis. The probable reasons for this failure are: (1) There is not enough reaction around the pulmonary lesions to cast shadows, (2) lesions may be located in the 25% of the lung obstructed from view by shadows of the diaphragm, heart, etc, (3) lesions may be located elsewhere in the body.

Some of the dense homogenous shadows as described above are due to *atelectasis* caused by pressure of enlarged lymph nodes on bronchi, tuberculoma, retained excretions, etc.

Presence of *calcification* in lungs and/or hilum region is never pathognomonic. There are numerous conditions which result in calcification including primary tuberculosis, fungus infections, etc. They should never be regarded as tuberculous without supporting evidence.

The erythrocyte sedimentation rate is accelerated in febrile cases about the time sensitivity to tuberculoprotein can be detected. This persists for a few weeks, then gradually decreases, after which it is within normal limits. The sedimentation rate is changed in a similar manner by other conditions and in itself is not diagnostic. *Differential leukocyte counts* may be helpful, but changes produced by primary tuberculosis are also caused by other conditions and therefore are not diagnostic.

Bacteriology

Persons with primary pulmonary infiltrates usually have no sputum. Gastric and bronchial washings may contain tubercle bacilli for a short time. In some groups of cases organisms have been found in as many as 25%. Ligner recovered tubercle bacilli from gastric contents of an infant of seven months while the disease was in the preallergic stage—in fact 14 days before there was a tuberculin reaction or the lesion was located. Bacteriologists have discovered numerous acid fast saprophytes in nature which under the microscope have an appearance similar to that of tubercle bacilli. These occur in certain butter, soil and among the grasses; therefore, the finding of acid fast organisms in the sputum, gastric washings or any other material does not always indicate the presence of tubercle bacilli. This fact has complicated laboratory work, since observing acid fast organisms is only the first step in the laboratory procedure. Once they are found it becomes necessary to use the culture or the inoculation method or both to determine whether a given acid fast organism is pathogenic.

TREATMENT

The first infection type of tuberculosis is an extremely benign disease. After it is fully developed it pursues a retrogressive course no matter how much or how little treatment is administered. During the brief febrile stage the individual should be treated just as when fever is cause by other infections such as influenza. The disease is noncontagious except in the occasional case with coexisting acute bronchitis. Symptoms are present over such a short time that treatment can be carried out in the home. Rest in bed should be continued until the red cell sedimentation rate returns to normal. Special forms of treatment such as collapse therapy are of no value and may do harm.

Children with demonstrable primary pulmonary infiltrates at the Minneapolis Health Center were divided into three groups. The first consisted of those who went to sanatoriums, the second, of those admitted to a special school, and the third, of those who remained at home with no special treatment. We were unable to see any difference in the course of the disease regardless of whether they were treated as strict bed patients, attended a special school or remained active in homes.

Observation proved that any and all types of treatment do not effect the immediate prognosis of primary tuberculosis in any stage of its development since the disease is in itself benign. The crucial point is the prevention of the endogenous reinfection type which is often decidedly not a benign condition. However, we have not been able to obtain evidence to show that hospitalization, special

schools, camps, or other form of treatment for primary lesions has any influence upon the later development of reinfection type of disease

In recent years, a number of primary pulmonary infiltrates with visible x-ray shadows have been treated with antituberculosis drugs However, they or enlarged regional lymph nodes apparently have not subsided more rapidly than has frequently been observed in the absence of drugs In no such case has there been reported reversion of sensitivity to tuberculin

When the lymph node component of the primary tuberculosis complex becomes so large and exerts enough pressure to close bronchial lumina thus resulting in atelectasis, there is the possibility of non tuberculous infections developing in the atelectatic areas followed by bronchiectasis However, this evidently occurs in only a small percentage of such cases In addition to antituberculosis drugs, x ray treatment has been tried in an attempt to shrink the lymph nodes enough to relieve pressure However, this has not proved entirely satisfactory In severe and prolonged cases, the bronchoscopist may temporarily establish air passage through the obstructed bronchial ramifications Surgical removal of large nodes may be considered

Recently some of the larger primary pulmonary infiltrates have been resected under antituberculosis drug protection Whether this is indicated can be determined only by long periods of observation Although such infiltrates nearly always resolve without treatment, necrotic areas harboring tubercle bacilli may remain If these areas are large, there may be some advantage in resecting them, since they may later result in endogenous reinfections However, the removal of primary pulmonary infiltrates by no means cures tuberculosis, inasmuch as there remain in the body numerous other primary lesions, both in the lungs and in extrathoracic locations, one or more of which may later result in endogenous reinfections

Antituberculosis drugs are now being administered to *recent tuberculin converters* This was proposed by Warring because it had always seemed illogical not to start treatment of an infectious disease as soon as the condition could be detected His proposal was adopted by a good many physicians who have since administered one or more of the antituberculosis drugs to recent tuberculin converters, both children and adults It was even hoped that long administration of drugs might result in such suppression of tubercle bacilli that they would ultimately die

Others are of the opinion that such drug treatment of recent converters is indicated even if it does not have germicidal effect This is on the basis that if the bacilli are well suppressed over a period of 6 months or more, there should not be much likelihood of early development of acute reinfection forms of tuberculosis such as miliary, meningitis, pneumonia and pleural effusion Although these acute forms are relatively rare among recent converters percentage-wise, it was thought worth while by some physicians to treat all such persons with the hope of preventing the few acute endogenous reinfections that might occur

Inasmuch as most recent converters, both children and adults, present no symptom, abnormal physical sign, or x-ray shadow, the only criterion by which one might determine effectiveness of the drugs would be reversion of the tuberculin reaction Reversion has been observed in a number of cases However, it is impossible to know whether all bacilli in their bodies are dead or are only suppressed to such low level that they are not eliminating enough tuberculoprotein to maintain allergy Discouraging evidence is accruing Hobby et al reported that tubercle bacilli from resected lesions of persons who have had long courses of antituberculosis drugs do not immediately grow in the usual culture medium or produce disease in guinea pigs However, if the cultures are allowed to incubate for 9 to 12 weeks, colonies begin to appear, indicating that the organisms have been revived They say, "From the data presented, it is apparent that tubercle bacilli can survive in healed or semi healed necrotic pulmonary lesions, even after prolonged chemotherapy and that, in many instances, their viability can be demonstrated by appropriate cultural techniques" Using liquid culture medium with

prolonged incubation resulted in growth of tubercle bacilli from 58% of lesions

Hall *et al* found that approximately one third of solid tuberculous lesions removed from persons after prolonged combined chemo



Fig 4 From a roentgenogram taken July 1947 of the chest of a student of nursing of 21 years Note evidence of extensive disease right lower lung field and hilum She entered a school of nursing as a nonreactor to tuberculin in 1944 In February and March 1947 she took training in a sanatorium In June 1947 she reacted to tuberculin and x ray film

The diagnosis was primary tuberculous infiltrates She was discharged to her home until after delivery She returned in March 1948 to complete nursing course Since graduation she has lead a normal life (From Myers Boynton and Diehl *Journal Lancet* May 1957)

therapy yielded viable tubercle bacilli by culture on egg medium or by guinea pig inoculation They later compared three methods of isolation of viable tubercle bacilli with similar volumes of hemogenized tuberculous lesions removed surgically after the "target point" had been reached with prolonged combined chemotherapy The three methods include guinea pig inoculation prolonged incubation for nine months in Lowenstein Jensen egg medium as well as Dubois liquid medium without Tween The material consisted of 65 solid nodular lesions Although acid fast bacilli were found in 76% only 20% produced tubercle bacilli by culture or guinea



Fig 5 Made from roentgenogram taken of same chest as seen in Figure 4 May 1955 when the ages of her five children were 7½ 6 5 3½ and 2 years Through all of this my health has been excellent " (From Myers Boynton and Diehl *Journal Lancet* May 1957)

pig inoculation Prolonged incubation of cultures produced growth in only three instances at 3 3 and 6 months each

From these data it seems likely that some persons who are treated because of recent tuberculin conversion and later present reversion of sensitivity may again become reactors to tuberculin some months after the discontinuance of antituberculosis drugs Thus the only advantage would have been a period of suppression of bacilli during which they may not have resulted in endogenous reinfections

Even if present drugs in various combinations and with long periods of administration do not prove germicidal a valuable treatment pattern has been established by which better future drugs may be administered

When one applies the tuberculin test to older children and adults who have not been previously tested with tuberculin there is no

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effective procedures have consisted of accurate early diagnoses prompt isolation of contagious cases in sanatoriums and hospitals periodic examinations of all adult tuberculin reactors close observation of those whose disease was previously arrested and rehabilitation in an effort to prevent reactivations and contagion More recently antituberculosis drugs and resectional surgery have contributed to the program of corralling and destroying *tubercle bacilli*

Veterinarians have so nearly eradicated tuberculosis from cattle in some parts of the world that it has become rare for people to acquire the bovine type of tubercle bacilli Contagious disease technique is practiced so well that in many tuberculosis hospitals and sanatoriums patients do not transmit tubercle bacilli to personnel or visitors Wherever good fundamental tuberculosis work has been done for a few decades the incidence of infection among children and young adults is low In some places the annual infection attack rate is a third of one per cent or less Testing of large numbers of pre school children results in finding the rare reactor Throughout grade school 2 or 3% and by the senior year in high school 4 or 5% react Among grade school children in Minneapolis 70% reacted to tuberculin in 1916 47% in 1926 19% in 1936 8% in 1944 and 4% in 1954 (Fig 6) In some colleges and universities less than 10% of entering students react to tuberculin From 1949 to 1951 Palmer *et al* tested more than 120 000 white men and women 17 to 21 years of age with an intermediate dose of tuberculin (0 0001 mg) Those tested included Navy recruits from all parts of the United States as they entered the Naval Training Center at San Diego California and students mostly freshmen attending colleges and universities in 17 states Only 8 3% reacted Among the recruits the percentage ranged from 20 among lifetime residents of Arizona and New Mexico to less than 4 in Idaho and Nebraska In parts of the world where less effective tuberculosis control programs have been in effect, the percentage of reactors among children and young adults is appreciably higher

Even in areas where good tuberculosis control work has been done over the last two or three decades one finds a relatively high percentage of persons in the upper age bracket reacting to tuberculin County wide tuberculin testing of persons of all ages from childhood through old age in a so-called low tuberculosis incidence county by Jordan and Jordan revealed only 1 3% of pre-school children with a gradual increase year by year to 7 3% of seniors in high school with an average of 4% whereas among women between 60 and 69 years 50 8% and among men of the same age 59 3% reacted Persons in the upper age brackets were not protected from tubercle bacilli in early life Many of them are still harboring residuals of infections acquired in childhood However those in the first few decades of life have been protected from invasions of tubercle bacilli by isolation of persons with contagious disease in sanatoriums pasteurization of milk well nigh eradication of tuberculosis among cattle etc

As soon as the tubercle bacillus was identified physicians and scientists set out to increase the resistance of animals against this organism *Dead tubercle bacilli* of different types killed by chemical agents light and heat have been administered but they proved unsuccessful *Living tubercle bacilli* of all types and of various degrees of virulence have been introduced into the bodies of large numbers of animals and humans in attempts to immunize them

From extensive experimental work in the latter part of the Nineteenth Century it was concluded that tuberculosis differs with reference to resistance produced from some of the other diseases It was known that an attack of smallpox results in considerable protection against subsequent attacks whereas a bout with tuberculosis confers no dependable immunity Despite this experimental work so well done and so frequently confirmed subsequently there have been those persons who have stoutly maintained that it should be possible to artificially develop resistance in the human body by first introducing living tubercle bacilli with lowered virulence or dead tubercle bacilli or individual fractions of these organisms Therefore one person after another has come forth with preparations each

way to determine how long ago the reactors were infected Therefore, even if a thoroughly germicidal drug were available, it probably would not be indicated in such cases because tuberculous lesions lose their blood supply After this has occurred, one could not hope that a germicidal drug, even in high concentration in the blood stream, would be able to enter avascular, necrotic areas and destroy all tubercle bacilli

PROGNOSIS

Prognosis in the first infection type of tuberculosis, *per se*, is excellent *In fact, during 37* years of observation of individuals with this type of disease at the Minneapolis Health Center and elsewhere, we have not seen one *person who died from it or have we ever seen* it cause serious illness

It has been stated that the prognosis should be guarded when the first infection type tuberculosis develops in *adult life* Over the years we have had an opportunity to observe more than two thousand persons who became reactors to tuberculin in adulthood In most of them there was a definite history of exposure to contagious cases of tuberculosis, prior to which they had been nonreactors, but following which they converted The course of the disease in these adults was essentially the same in every respect as we had seen in children (Figs 4 and 5)

Among northern Negroes and American Indians we have observed that the body defends [illegible] first infection type of tubercu-

races and among white adults, a question *arises concerning* the statement that the first infection type of tuberculosis is so destructive among adult Negroes, Indians, Mexicans etc As far as we have been able to determine, statements made to this effect have not been based *upon* longitudinal studies of the same individuals, that is, the antecedent history of infection and allergy is not known One must, therefore, inquire as to whether these destructive forms of tuberculosis are *not* reinfections rather than first infections It appears that in the various animal species studied and in humans, *regardless of race*, nationality, or age, the same defense mechanism attacks tubercle bacilli of first infection, *and in the human* body, the bacilli are so well under control when allergy appears that little destruction occurs unless bacilli are later set free and find lodgment in sensitized tissues where they set up *reinfection forms of disease*

Despite the fact that prognosis in the first infection type of tuberculosis is excellent, it sets the stage for every form of destructive reinfection type of tuberculosis that develops *in humans Therefore, the ultimate prognosis,* as far as clinical tuberculosis is concerned, may be unfavorable in a considerable percentage of persons who at the moment, have only the primary type of the disease

PREVENTION

Avoid Initial Infection

The only present available way to prevent the first infection type of tuberculosis from developing in people is to create an environment which is free from contagious cases of tuberculosis both among humans and animals There is no evidence whatsoever that special diets, rest schedules, etc, prevent the development of primary tuberculosis complexes if tubercle bacilli are permitted to enter Moreover, once the lesions of primary tuberculosis complexes are established, *we have no control* over them The allergy they produce continues as long as the tubercle bacilli remain alive, and, as yet, there has not been devised a practical method of desensitizing the tissues *The tubercle bacilli they harbor serve* as a constant threat to future health The best known diet and even strict bed rest does not prevent development of the reinfection forms of tuberculosis in such persons *If tubercle bacilli are not permitted to enter, there can be* no primary tuberculosis complexes or subsequent clinical lesions It is not until this situation obtains among all the people and animals

fected persons has markedly decreased The

claiming superiority of his own over all others Koch presented tuberculin von Behring bovovaccine and Calmette Bacillus Calmette Guerin (BCG) etc

During the 70 years that such agents have been continuously in use none has passed the experimental and highly controversial stage There has been no premise for such efforts inasmuch as an attack of tuberculosis mild or severe confers no dependable immunity against subsequent reactivation and evolution of new lesions in the human body There is an abundance of evidence to demonstrate how these agents have retarded tuberculosis eradication programs such as

(1) They give individuals and populations false sense of security resulting in relaxation of other efforts against the tubercle bacillus

(2) When living tubercle bacilli such as BCG are administered multiple focalizations and primary lesions are produced just as when natural invasions occur Thus the early pathogenesis of tuberculosis is enacted

(3) During the development of multiple primary lesions produced by BCG tissues become sensitized to tuberculoprotein This retards progress because (a) it eliminates the future use of the tuberculin test in diagnosis epidemiology etc and (b) allergy is a dangerous factor in the event of subsequent infection

(4) There is no evidence that these agents prevent subsequent invasions of tubercle bacilli from natural sources

(5) BCG itself results in enough abscesses and ulcers at the site of administration and serious lymphadenitis which requires treatment as well as numerous other lesions including lupus vulgaris as to be alarming

(6) Well documented cases are now on record of deaths having been caused by BCG

Drugs

Thus the only known method of preventing primary tuberculosis consists of avoiding tubercle bacilli Once they enter the body, they usually produce at least microscopical lesions Recent observations on drugs as preventive measures have opened a field which needs thorough investigation For example Schmidt administered isoniazid to 51 rhesus monkeys which did not react to tuberculin While on this drug they were exposed to tuberculous monkeys and even those with the longest exposure (9 months) did not become tuberculin reactors Of the entire 51 at the beginning of the experiment 5 died from nontuberculous conditions and 17 were sacrificed for histopathological studies In the absence of drugs rhesus monkeys nearly always become positive to tuberculin or are dead within 9 months after exposure to other tuberculin positive animals

Ferebee and Palmer gave guinea pigs isoniazid and later introduced virulent tubercle bacilli If isoniazid was continued for only 10 weeks after bacilli were admitted it prevented mortality from tuberculosis for at least the 26 weeks the animals were observed the animals grew in weight at the same rate as normal untreated uninfected guinea pigs

On the basis of such observation it appears to be possible that if drugs are present tubercle bacilli which invade the body may be prevented from gaining a foothold

CLINICAL (REINFECTION TYPE) TUBERCULOSIS

The reinfection type of tuberculosis is dependent for its development on the presence of the first infection type Apparently innocuous lesions of primary complexes may at any time have their capsules (including calcium and bone) resorbed and the pent up bacilli liberated Implantations of tubercle bacilli on allergic tissues are responsible for practically all of the acute and chronic destructive clinical tuberculosis While the defense mechanism succeeds at least temporarily with many reinfections it fails often enough to account for all the illness and death from tuberculosis among the people of the world Obviously therefore humans possess a defense mechanism that protects far more effectively against the first invasion of tubercle bacilli than against subsequent attacks

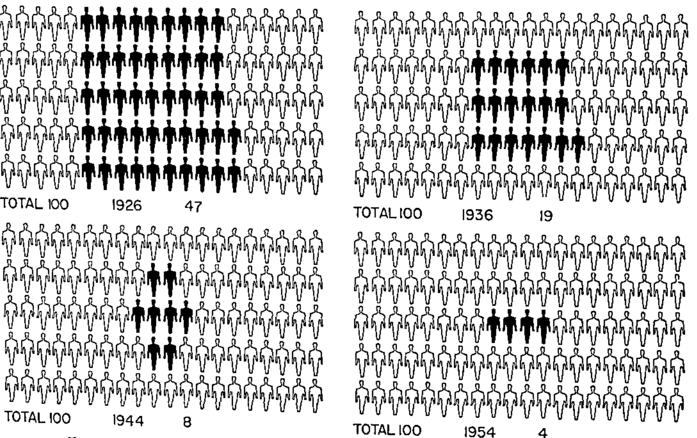


Fig 6 Shows results of testing children in the same grade schools approximately every 10 years These schools were selected in 1926 geographically so as to represent the childhood population of the city The numbers of tuberculin reactors (black figures) per 100 children are shown for the years, 1926, 1936, 1944 1954 (*From Myers et al J A M A*, 1955)

complexes This erroneous concept resulted from conclusions drawn without sufficiently long periods of observation The reaction in the vicinity of reinfections is so intense and tuberculoprotein so poisonous that it is impossible for individual neutrophils to ingest and distribute bacilli to other places where, in small numbers the defense mechanism would be more likely to succeed Thus when large numbers of tubercle bacilli are suddenly discharged on allergic lung tissue acute tuberculous pneumonia results When smaller numbers of tubercle bacilli invade allergic lung tissue the defense mechanism may operate more successfully so as to reduce and hold the lesions in chronic smoldering stages

The reinfection type of pulmonary tuberculosis may develop at any time after the tissues become sensitized and tubercle bacilli from any source find lodgment in them it may also appear in any part of the body This type of tuberculosis occurs in two main forms (1) *acute lesions* some of which progress rapidly to fatal termination while others after passing through an acute stage gradually subside (2) *chronic lesions* which usually begin in a small way and progress slowly

ACUTE FORMS

The fatal acute forms of reinfection type of tuberculosis include miliary disease pneumonia and meningitis For a long time these were thought to represent the first infection type of tuberculosis since individuals who were apparently in excellent health suddenly fell ill from these forms of the disease There had been no opportunity to examine them with reference to tuberculosis while they were well However observation has revealed that when the tuberculin test is administered routinely and periodically the first infection type of tuberculosis can be detected before the acute reinfection forms of disease develop Moreover carefully performed postmortem examinations reveal the primary lesions In this manner it has been shown that our original impressions were wrong and that when an individual falls ill or dies from acute forms of tuberculosis they have always been preceded by the first infection type of disease which set the stage for their development.

Generalized Miliary Tuberculosis

Generalized miliary tuberculosis is caused by pre existing tuberculous lesions (often parts of primary complexes) which erode through walls of blood vessels or large lymphatic ducts and discharges their contents into the blood or lymph stream Again there may be direct tuberculous invasion of the walls of vessels Operations on tuberculous bones joints and other parts of the body may also allow large numbers of organisms to enter the blood stream

Rarely does miliary tuberculosis develop in more than 1% of persons suffering from chronic pulmonary tuberculosis It is more likely to appear among persons who have had no previous experience with clinical disease Therefore more cases originate in homes and general hospitals than in sanatoriums

Whenever large numbers of tubercle bacilli reach the blood stream the organs richly supplied with fine capillaries filter out many of the organisms The tissues are already allergic by reason of the previous development of primary complexes and therefore wherever bacilli lodge their protein content is a violent poison to cells and tissues and an intense specific reaction occurs

The resulting tubercles usually are of approximately the same age and extent of development In addition to large numbers in the lungs others may be found in such organs as kidneys liver spleen and brain The number of tubercles is so great that the condition is overwhelming and formerly caused death in a few weeks or months Generalized miliary tuberculosis may occur at any time in life but is more likely to develop within a few years after primary tuberculosis appears

Diagnosis *History of exposure* to persons with contagious tuberculosis is important however in many cases such history is not known It is often possible to locate the previously unsuspected individuals by examining the adult associates of the patient

Symptoms These consist of weakness malaise and fever usually mild in the beginning but increase in severity as the disease

Allergy to tuberculoprotein accounts for failures to protect against reinfections. This protein released from tubercle bacilli of first invasion organisms (before allergy appears) is innocuous. It offers no handicap to the defense mechanism. However, after allergy is established, tuberculoprotein becomes a violent poison to cells and tissues. Experimental tissue culture studies have revealed that leucocytes from animals which had not been infected with tubercle bacilli were not harmed when they were brought in contact with tuberculin, whereas those from animals with tuberculosis were definitely damaged under the same treatment. Rich and Lewis used hundreds of cultures of leukocytes and of spleen and demonstrated that the cells obtained from tuberculous animals were killed by amounts of tuberculin in which cells from normal animals grew freely.

Seibert sensitized normal guinea pigs by weekly intracutaneous injections of 10 mg. of tuberculoprotein of large molecular size. Subsequent studies of these animals showed that there existed a high degree of sensitiveness without any specific immunity or increased resistance to tubercle bacilli. On the contrary, it seems to hasten and extend the lesion and to be associated with much more extensive necrosis and caseation than is found in unsensitized animals.

The studies of Lemon and Montgomery with reference to the effects of sensitiveness of the tissues on the development of destructive forms of tuberculosis are significant. The conclusions of their extensive experimental work are as follows: "When virulent organisms of Mycobacterium tuberculosis (bovis) are introduced into pleural spaces of healthy rabbits they constitute foreign bodies of the particulate type to which tissues react with a nonspecific form of inflammation. The fluid and cellular parts of the resultant effusion are promptly resorbed, carrying with them the particulate material which had been phagocytosed and depositing it in regional lymph nodes and in remote organs. Many of the intracellular bacilli could not be removed but remained within the lymph spaces or were included in cellular masses attached to the pleural surface. Up to this point the reaction is entirely nonspecific. Thereafter it becomes specific because the particulate matter is made up of living organisms and is capable of growth and division. Nonsensitive tissues are changed to sensitive tissues and allergic reactions respond to reinfection as vast numbers of virulent bacilli are released into the tissues. The massive persisting effusions are objective evidence of a specific response to reinfection.

"Tubercles develop on pleural surfaces as a result of persisting irritation of residual bacilli and represent hyperplasia of histiocytes and regional fibroblasts. Epithelioid cells and giant cells appear as developmental changes in histiocytes. Similar tubercles develop in the parenchyma of the lung, in the regional nodes and in the remote organs wherever residual bacilli are harbored and are increased in numbers by growth of organisms. Caseation and ulceration of tubercles into the lumen of bronchi and veins constitute hazards to the life of the animal by providing a means of rapid transport of organisms to uninfected tissues. The acute reactions and the lesions which bring about illness and death are final evidences of a specific reaction." In 1943, after further study, Lemon and Feldman said:

... we are of the opinion that a sensitized pleura and living bacilli in the pleural space are requisite factors in the production of experimental tuberculous pleural effusion.

Tubercle bacilli of reinfection require much more effort on the part of the defending elements and the response of the white blood cells is greater in point of numbers than in primary infections. In fact, the response is so great that large numbers of tubercle bacilli are temporarily held at their sites of invasion. This often results in serious destructive situations in that so many bacilli are present and so much tuberculoprotein is liberated in one place as to destroy the adjacent defending cells as well as the fixed tissues in the immediate vicinity. Thus, areas of necrosis of varying size are produced. It is this temporary fixation of tubercle bacilli of reinfection at their sites of invasion that was long misinterpreted as representing resistance thought to have been built up by the presence of tubercle bacilli in lesions of primary tuberculosis.

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Allergy to tuberculoprotein *accounts for failures* to protect against reinfections. This protein released from tubercle bacilli of first invasion organisms (before allergy appears) is innocuous. It offers no handicap to the defense mechanism. *However after allergy is* established tuberculoprotein becomes a violent poison to cells and tissues. Experimental tissue culture studies have revealed that leucocytes from animals which had not been infected with tubercle bacilli *were not harmed* when they were brought in contact with tuberculin whereas those from animals with tuberculosis were definitely damaged under the same treatment. Rich and Lewis used hundreds of cultures of leukocytes and of spleen and demonstrated that the cells obtained from tuberculous animals were killed by amounts of tuberculin in which cells from normal animals grew freely.

Seibert sensitized normal guinea pigs by weekly intracutaneous injections of 10 mg of *tuberculoprotein of large molecular size.* Subsequent studies of these animals showed that there existed a high degree of sensitiveness without any specific immunity or increased resistance to tubercle bacilli. On the contrary "*it seems to hasten and extend the lesion and* to be associated with much more extensive necrosis and caseation than is found in unsensitized animals."

The studies of Lemon and Montgomery with reference to the effects of sensitiveness of the *tissues on the development of destructive* forms of tuberculosis *are significant. The con*clusions of their extensive experimental work are as follows: "When virulent organisms of Mycobacterium tuberculosis (bovis) are introduced into pleural spaces of healthy rabbits *they constitute foreign* bodies of the particulate type to which tissues react with a nonspecific form of inflammation. *The fluid and* cellular parts of the resultant effusion are promptly resorbed, carrying with them the particulate material which had been phagocytosed and depositing it in regional lymph nodes *and in remote organs.* Many of the intracellular bacilli could not be removed but remained within the *lymph spaces or were in*cluded in cellular masses attached to the pleural surface. Up to this point the reaction is entirely nonspecific. Thereafter it becomes specific because the particulate matter is made up of living organisms and is capable of *growth and division.* Non-sensitive tissues are changed to sensitive tissues and allergic reactions respond to reinfection as vast numbers of virulent bacilli are released into the tissues. The massive persisting effusions are objective *evidence of a specific response to reinfection.*

"*Tubercles develop* on pleural surfaces as a result of persisting irritation of residual bacilli and represent hyperplasia of histiocytes and regional fibroblasts. Epithelioid cells and giant cells appear as developmental changes *in histiocytes. Similar tubercles develop in the* parenchyma of the lung, in the regional nodes and in the remote organs wherever residual bacilli are harbored and are increased in numbers by growth of organisms. Caseation and ulceration of tubercles into the lumen of bronchi and veins constitute hazards to the *life of the animal by providing a means of* rapid transport of organisms to uninfected tissues. The acute reactions and the lesions which bring about illness and death are final evidences of a specific reaction." In 1943 *after further study* Lemon and Feldman said: "... we are of the opinion that a sensitized pleura and living *bacilli in the pleural space* are requisite factors in the production of experimental tuberculous pleural effusion."

Tubercle bacilli of reinfection require much *more effort* on the part of the defending elements and the response of the white blood cells is greater in point of numbers than in primary *infections. In fact, the response is* so great that large numbers of tubercle bacilli are temporarily held at their sites of *invasion.* This often results in serious destructive situations in that so many bacilli are present and so much tuberculoprotein is liberated in one place as to destroy the adjacent defending *cells as well as the fixed tissues* in the immediate vicinity. Thus areas of necrosis of varying size are produced. *It is this temporary* fixation of tubercle bacilli of reinfection at their sites of invasion that was *long mis*interpreted as representing resistance thought to have been built up by the presence of tubercle bacilli in lesions of primary tuberculosis.

complexes This erroneous concept resulted from conclusions drawn without sufficiently long periods of observation The reaction in the vicinity of reinfections is so intense and tuberculoprotein so poisonous that it is impossible for individual neutrophils to ingest and distribute bacilli to other places where, in small numbers, the defense mechanism would be more likely to succeed Thus when large numbers of tubercle bacilli are suddenly discharged on allergic lung tissue, acute tuberculous pneumonia results When smaller numbers of tubercle bacilli invade allergic lung tissue the defense mechanism may operate more successfully so as to reduce and hold the lesions in chronic smoldering stages

The reinfection type of pulmonary tuberculosis may develop at any time after the tissues become sensitized and tubercle bacilli from any source find lodgment in them it may also appear in any part of the body This type of tuberculosis occurs in two main forms (1) *acute lesions* some of which progress rapidly to fatal termination while others after passing through an acute stage gradually subside (2) *chronic lesions*, which usually begin in a small way and progress slowly

ACUTE FORMS

The fatal acute forms of reinfection type of tuberculosis include miliary disease pneumonia and meningitis For a long time these were thought to represent the first infection type of tuberculosis since individuals who were apparently in excellent health suddenly fell ill from these forms of the disease There had been no opportunity to examine them with reference to tuberculosis while they were well However observation has revealed that when the tuberculin test is administered routinely and periodically the first infection type of tuberculosis can be detected before the acute reinfection forms of disease develop Moreover, carefully performed postmortem examinations reveal the primary lesions In this manner it has been shown that our original impressions were wrong and that when an individual falls ill or dies from acute forms of tuberculosis they have always been preceded by the first infection type of disease which set the stage for their development

Generalized Miliary Tuberculosis

Generalized miliary tuberculosis is caused by pre existing tuberculous lesions (often parts of primary complexes) which erode through walls of blood vessels or large lymphatic ducts and discharges their contents into the blood or lymph stream Again there may be direct tuberculous invasion of the walls of vessels Operations on tuberculous bones joints and other parts of the body may also allow large numbers of organisms to enter the blood stream

Rarely does miliary tuberculosis develop in more than 1% of persons suffering from chronic pulmonary tuberculosis It is more likely to appear among persons who have had no previous experience with clinical disease Therefore more cases originate in homes and general hospitals than in sanatoriums

Whenever large numbers of tubercle bacilli reach the blood stream the organs richly supplied with fine capillaries filter out many of the organisms The tissues are already allergic by reason of the previous development of primary complexes and therefore wherever bacilli lodge their protein content is a violent poison to cells and tissues and an intense, specific reaction occurs

The resulting tubercles usually are of approximately the same age and extent of development In addition to large numbers in the lungs others may be found in such organs as kidneys liver spleen and brain The number of tubercles is so great that the condition is overwhelming and formerly caused death in a few weeks or months Generalized miliary tuberculosis may occur at any time in life but is more likely to develop within a few years after primary tuberculosis appears

Diagnosis *History of exposure* to persons with contagious tuberculosis is important however in many cases such history is not known It is often possible to locate the previously unsuspected individuals by examining the adult associates of the patient

Symptoms These consist of weakness malaise and fever usually mild in the beginning but increase in severity as the disease

progresses The temperature ranges from 101 to 104°F with proportionate increase in the pulse rate The respiratory rate may be normal at first but later becomes markedly increased and cyanosis may be severe in the late stage of the disease Cough is absent or slight *in the beginning but later becomes distressing* Sputum usually is scant or absent No symptom is pathognomonic

Abnormal signs are rarely elicited by *palpation percussion or auscultation* On *inspection* of the surface of the body the patient appears seriously ill and as the disease progresses toxemia cyanosis and dyspnea may become extreme X ray film inspection of the chest usually is not helpful in the beginning of the disease However in the late stage in *approximately 50% of cases* a large number of small shadows appear which are cast by the miliary tubercles Steiner found the *x* ray film reveals evidence of the disease only when tubercles contain caseous material or collagen When shadows are seen it is impossible to differentiate them from those cast by other conditions such as sarcoidosis carcinomatosis silicosis multiple pyemic small abscesses leukemic infiltrations of miliary form disseminated influenzal pneumonia bilharziasis idiopathic *progressive brown induration* where the minute spots seen in the film are due to hemosiderosis caused by recurring hemorrhage diffuse myomatosis or fibrosis with formation of cysts miliary densities associated with mitral stenosis etc Many cases of bronchiolitis have been wrongly diagnosed as miliary tuberculosis *from x ray films*

Ophthalmoscopic examination may reveal the presence of tubercles in the retina even though x ray films of the chest are clear

Examination of *sputum* usually is of no aid until the last few days of the patient s life if at all since death often occurs before there is sufficient time for the lesions to break down so as to liberate tubercle bacilli

In every case of miliary tuberculosis the tissues are sensitized to tuberculoprotein and therefore if tested will react to tuberculin before the disease manifests itself However as it progresses the tissues may become desensitized so they fail to react to the usual doses

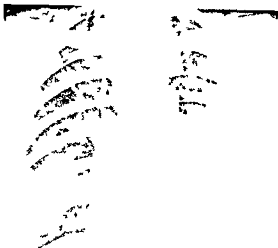


Fig 7 From a roentgenogram taken November 1951 of the chest of a woman of 56 years A quarter of a century before her husband had contagious tuberculosis She then reacted to tuberculin X ray films were made of her chest periodically None had shown evidence of significant disease until November 1951 The lesion in the *left lower lung field is tuberculous pneumonia*

In 1946 Schleicher demonstrated that examination of bone marrow often reveals the presence of tuberculous granulomata in per*sons who have generalized miliary tuberculosis* These lesions contain tubercle bacilli which can be stained and which produce colonies in culture medium and disease in guinea pigs This finding is pathognomonic

Pneumonia

This disease is always preceded by the first infection type of tuberculosis It may result from a lesion of a primary complex eroding into an air passage and discharging its contents into the lumen Some of this material is aspirated into the finer bronchioles and the alveoli It is also possible that a primary *focus may rupture so that numerous tubercle* bacilli are disseminated in the region of the original focus resulting in intense specific reaction in this area Chronic reinfection types of pulmonary lesions may disseminate tubercle bacilli in the same manner and set up tuberculous pneumonia

With the tissues already allergic an in se specific reaction results (Fig 7) This

may involve a segment a lobe or an entire lung The intense reaction may be likened to that seen in the skin of an allergic person 48 to 72 hours after tuberculin has been introduced intracutaneously Thus a lung which is entirely clear to all phases of an examination may within a few days after tubercle bacilli invade present evidence of extensive disease When large areas of pulmonary tissue are involved tuberculoprotein is so poisonous that necrosis occurs promptly In a short time large amounts of necrotic tissue may be expectorated leaving pulmonary cavities

In the beginning the disease may closely simulate usual lobar or bronchopneumonia Tuberculous pneumonia has often been misdiagnosed as primary tuberculosis because it suddenly appears in persons previously apparently in excellent health It constitutes the first manifestation of tuberculosis probably this is the reason that primary tuberculosis was formerly thought to be so fatal in infants and young children Tuberculous pneumonia in infancy or at any other age in life is preceded by primary lesions which usually have caused no illness and have gone unrecognized until the reinfection in the acute form appears When one has an opportunity to observe infants and children one is usually able to detect by the tuberculin reaction the presence of primary tuberculosis well in advance of the appearance of pneumonia Therefore tuberculous pneumonia is a reinfection form of tuberculosis The primary disease has set the stage by retaining in its lesions living virulent tubercle bacilli which are the sources of endogenous reinfection and by causing the tissues to become allergic to tuberculoprotein

Diagnosis The onset may be insidious with first *symptoms* consisting of mild cough slight temperature elevation aching of the body loss of appetite and malaise In a short time however the symptoms are markedly accentuated body weight loss is rapid cough becomes severe and sputum markedly increases in amount changing from clear mucous to yellowish or greenish color Streaks of blood in the sputum and even frank hemorrhage are not uncommon When the pleura becomes involved chest pain is a frequent symptom In some cases the onset is extremely sudden starting with chills and high fever and almost immediately the individual appears desperately ill Following this symptoms are essentially the same as in those with an insidious onset

On examination *palpation percussion* and *auscultation* reveal findings identical with those of other types of pneumonia In many cases cavity signs soon become apparent *Inspection* of the surface of the body usually reveals a desperately ill individual Often the cheeks are flushed and the respiratory rate is increased profuse sweating and chills may be observed X ray film inspection reveals evidence of infiltration consolidation and in many cases cavitation

Tubercle bacilli may not be recovered during the first 10 days to 2 weeks after the onset of symptoms Usually it is only when they appear that the diagnosis is made For this reason in every case of pneumonia regardless of what the etiology may prove to be the sputum should be examined for tubercle bacilli

Meningitis

By meticulous examination of brains and spinal cords of persons who had died from tuberculous meningitis Rich and McCordock always found pre existing lesions often containing calcium in or adjacent to the central nervous system These lesions apparently had caused no previous symptom until nature paradoxically treated them as foreign bodies and resorbed their walls thus liberating tubercle bacilli into ventricles or subarachnoid spaces Lodging an allergic meninges in such large numbers resulted in an intense specific inflammation in such a vital part as to always be incompatible with life until suppressive drugs became available

Prior to these observations tuberculous meningitis was thought to result from an initial attack of tubercle bacilli and hence the primary type was said to be highly destructive In reality the original central nervous system lesions had pursued a benign course as they do elsewhere in the body but they

harbored the tubercle bacilli that resulted in the endogenous reinfection

Diagnosis Tuberculous meningitis always occurs in persons who are *sensitive to tuberculin* However, if the test is not administered until the disease is well under way failure to elicit a characteristic reaction may be misleading This is because acute serious forms of tuberculosis often result in partial desensitization of tissues Recovery of tubercle bacilli from spinal fluid is the only other specific finding In a relatively small percentage of cases tubercle bacilli may not be found in one or more specimens of spinal fluid

Treatment of Acute Forms

Generalized miliary tuberculosis and meningitis were universally fatal and pneumonia often was before antituberculosis drugs became available

If antituberculosis drugs are promptly administered early spectacular results may be observed in most cases Symptoms rather promptly disappear and at least temporary recovery is often observed

When these conditions are diagnosed the situation is so desperate that many physicians prefer to promptly administer all three of the major antituberculosis drugs At least 1 gm of streptomycin is introduced intramuscularly daily for 1 or 2 weeks and then semiweekly as long as indicated The damage *streptomycin may cause to the eighth cranial* nerve must be kept in mind and hence the importance of decreasing frequency of administration as soon as indicated Para amino salicylic acid is given by mouth 12 gm daily divided into four equal doses for adults Isoniazid is administered *by mouth 5 to 8 mg per* kg of body weight in three or four equal doses daily When the patient apparently is *out of immediate danger one of the drugs* preferably streptomycin may be discontinued

The above doses are for adults For children they should be scaled down according to well known dosage rules

When antituberculosis drugs were administered for only a few months the relapse rate was high Prolonged administration has been found much more satisfactory and therefore drugs are usually continued for at least 1 year and many physicians prefer 18 months to 2 years

Isoniazid apparently penetrates tissues of *the nervous system* more effectively than the other two drugs In fact it has been found so effective in treating meningitis that some *physicians now prefer to use it as the only* drug However, combined drugs seem more advisable

Corticotropin *or cortisone have been* employed in acute, inflammatory forms of tuberculosis Using the rabbit ear chamber technique Ebert found three consistent changes produced in the inflammatory reaction which are common to other types of inflammations studied He says "First vascular tone is better maintained Second, there is a reduction in damage to arteriolar and venule endothelium Third as a result of the increased integrity of vascular endothelium there is a decrease in diapedesis of leucocytes and a reduction in exudate

Although cortisone delays tissue destruction the reduction in inflammation impairs localization of infection"

Johnson considers tuberculous meningitis as probably the best indication in tuberculosis for the administration of hormones He reported a case in which an interrupted course of corticotropin was used as an adjunct to streptomycin isoniazid and para-aminosalicylic acid He called attention to possible *danger of corticotropin or cortisone pointing* out that in addition to possibilities of aggravating the tuberculosis or decreasing the effectiveness of antituberculosis drugs *there is* always the possibility of causing fluid retention diabetes mellitus peptic ulcer etc *Therefore if used at all hormones* are employed in extreme cases and then with great care

Moreau (Paris) states that ACTH and cortisone often bring about decisive changes for the better in cases with poor prognosis Good response has been observed where antibiotics had not been helpful or were poorly tolerated He emphasizes the importance of avoiding too high dosage and simultaneously administering *antituberculosis drugs* *Even then* he says it is advisable to proceed with caution

Suppressive drugs should be administered

as early in the course of the disease as diagnosis is possible If the physician is first called late in the evolution of these conditions present drugs may be of little avail In meningitis the disease already has caused so much damage to the brain that even if a drug were available that would promptly kill all tubercle bacilli the victim would be suitable only for an institution for the mentally ill If the physician is called early and fails to make the diagnosis until such destruction has occurred to the brain the same failure in treatment is to be expected

Without treatment tuberculous meningitis and miliary disease are so fatal that if an individual known to be a reactor to tuberculin develops suggestive symptoms and no other etiological agent is found a presumptive diagnosis should be made and treatment instituted promptly If this is not done and necropsy reveals presence of tuberculosis litigation may be instituted

Although there are many persons children and adults now living who would have died without antituberculosis drugs there is no absolute assurance that these conditions may not later recur or is there any likelihood that all tubercle bacilli have been destroyed in the multiple lesions elsewhere in their bodies Therefore they must be kept under close surveillance with references to appearance of other clinical lesions at any future time

Prevention of Fatal Acute Forms

There is no dependable way of preventing the acute forms of tuberculosis except to avoid the initial invasion with tubercle bacilli Once these organisms pass any portal of entry and are ingested by neutrophils one has no control over the places in the body where focalizations will occur Once they are focalized there is as yet no sure method of preventing nature from later liberating bacilli from the encapsulated lesions

These forms of the disease may be caused by either the human or bovine types of tubercle bacilli The incidence of acute forms is dependent upon the percentage of persons harboring tubercle bacilli as manifested by the tuberculin reaction Wherever a higher percentage of infants and children react to tuberculin one may expect considerable acute disease among them This has been demonstrated in areas where a high percentage of children reacted to tuberculin a quarter or more of a century ago when such cases were available for the teaching of students of nursing and medicine at all times However in areas where good tuberculosis control programs have been in effect in both people and animals and the incidence of tuberculin reactors among children has been reduced to 2 or 3% fatal acute forms of tuberculosis have become rare Indeed in whole cities with populations of several hundred thousand a year or more passes without a single child developing acute tuberculosis In the same areas where the older adults did not have such protection as children and 50 to 60% react to tuberculin most of such cases are now seen among them

CHRONIC PULMONARY TUBERCULOSIS

The disease may be caused by the human, bovine and occasionally the avian type of tubercle bacilli In countries where tuberculosis has not been well controlled among cattle from 1 to 6 % of chronic clinical pulmonary lesions are due to the bovine type To date there have been approximately 25 well documented cases caused by the avian type It always develops in tissues sensitized by previous primary disease Approximately 85 to 90% of all chronic tuberculosis occurs in the lungs It is this form of the disease which is largely responsible for perpetuation of tubercle bacilli in both people and animals

Reinfection type of tuberculosis in the central nervous system the liver spleen pericardium pleura peritoneum as well as bones and joints is due to endogenous reinfections There has been controversy between those who believe that chronic clinical pulmonary tuberculosis is the result of endogenous reinfections and those who cling to the view that they are exogenous Long periods of observation on the same individuals definitely favor the endogenous source of tubercle bacilli for such reasons as (1) All persons who develop chronic clinical pulmonary tuberculosis have primary lesions harboring tubercle

bacilli in necrotic areas which may have been present only *for months or for decades*. (2) Nature may resorb the fibrous calcified or even osseous encasements of primary complex lesions and liberate tubercle bacilli on allergic tissues. (3) Persons with primary lesions as manifested by the tuberculin reaction have often had the responsible adult associates removed by death or to institutions with no known subsequent exposure but years or decades later presented chronic clinical disease. While there is no incontrovertible proof that subsequent exposure did not occur, close observation of immediate contacts revealed none. (4) In areas where a preponderance of chronic lesions now being found are in persons of the upper age brackets usually it has not been possible to find a recent contagious contact among their associates. Further evidence that such sources of exogenous reinfections do not exist is that tuberculin reactors among children and young adults of the communities have continued to decrease whereas one would expect an increase if contagious cases were in the community reinfecting the older people. Moreover, necropsies done with sufficient care on elderly persons who died from tuberculosis almost invariably reveal lesions of old primary complexes, some of which are still carrying necrotic tissue.

This is not to say that exogenous reinfections are impossible. It is well known that animals already sensitized to tuberculoprotein can be reinfected exogenously. Wherever a large number of persons with contagious tuberculosis are permitted to mingle with the population it has been assumed that they were responsible for many exogenous reinfections among their associates. How often this actually occurs is not known. However, in several sizeable areas where contagious cases mingling with the population have become relatively rare, the previously infected individuals, young and old, continue to develop chronic clinical pulmonary tuberculosis.

Stages of Disease

When one examines a large number of people in an area where much contagion has been allowed to exist, one finds those with pulmonary lesions barely demonstrable while at the opposite extreme are those with lesions involving nearly all parts of both lungs and practically every intermediate gradation is observed. The National Tuberculosis Association has produced a helpful brochure entitled *Diagnostic Standards and Classification of Tuberculosis* which contains the following classification with reference to extent of pulmonary lesions.



Fig. 6. From a roentgenogram of the chest taken March 16, 1951, of a woman of 45 years. Note evidence of lesion in right lung near periphery partially *obscured from view by right second rib anteriorly*. All previous x-ray films had been clear. She had been a tuberculin reactor for several years. This lesion proved to be a progressive tuberculous process. No significant symptom was present but tubercle bacilli were found in gastric washings. Nearly all chronic pulmonary lesions can be found in this early stage by periodically examining adult tuberculin reactors. These lesions may appear any time after the tissues are allergized throughout the remainder of the individual's life. (From Myers, Boynton and Diehl, *Journal Lancet*, May, 1957.)

Minimal Slight lesions without demonstrable excavation confined to a small part of one or both lungs The total extent of the lesions regardless of distribution shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side

Moderately advanced One or both lungs may be involved but the total extent of the lesions shall not exceed the following limits

Slight disseminated lesions which may extend through not more than the volume of one lung or the equivalent in both lungs

Dense and confluent lesions which may extend through not more than the equivalent of one third the volume of one lung

Total diameter of cavities less than 4 centimeters

Far advanced Lesions more extensive than moderately advanced

Diagnosis

Tuberculosis can be diagnosed in the minimal stage in 95% of cases by finding adults who react to tuberculin while the x ray films of their chests are clear and examining them periodically thereafter The tuberculin reaction is positive proof that tuberculosis is present Since it evolves to clinical proportions only in tuberculin reactors it is they who must be watched for its earliest appearance Where many persons both children and adults have been observed to become tuberculin converters and have been kept under close observation by periodical examinations including x ray film inspection of the chest it has been shown that clinical tuberculous lesions (except the exudative type which rarely exceeds 5% of the total) can be located when the shadows they cast are small (Fig 8)

While lesions usually first appear in the upper lung fields enough occur in other areas that an x ray shadow casting lesion in any part of the lungs of a tuberculin reactor may be tuberculous

Minimal lesions found by this method do not always progress but when they do and treatment is refused the rate of progression varies somewhat but is usually slow In fact in sizable groups the average has been approximately 2½ years after lesions are first detectable by the x ray shadows they cast before significant symptoms are present and tubercle bacilli are found in sputum By this time the lesions often are so extensive as to be classified advanced

Chronic lesions usually pass through a long silent period during which the host has no health complaint to suggest examination therefore it is important to make x ray film inspection of the chests of reactors periodically Since conventional physical examination is unavailing through most of this period it is essential that periodical x ray film inspection be done preferably on regular size films This reveals lesions as soon as they have adequate size consistency and location to cast visible shadows Until the lesions meet these qualifications they are missed by x ray film inspection Therefore a clear x ray film by no means denotes the absence of lesions

When clinical pulmonary tuberculosis progresses and is not treated it reaches an advanced stage The silent period with reference to appearance of significant symptoms sometimes continues into the moderately advanced and occasionally into the far advanced stage (Fig 9) When symptoms appear the disease is already in an advanced stage in about 85% of cases Therefore symptoms are usually a late manifestation of tuberculosis By this time the disease is likely to be contagious in that tubercle bacilli are recoverable from sputum

With rare exceptions (usually due to errors in technique) persons with advanced tuberculosis continue to react to tuberculin except when the terminal stage is approached At that time the tissues may become so desensitized that there is no reaction to the first dose or in some cases even the second In order to elicit a reaction a larger dose is necessary The tuberculin reaction is not so important at this time as tubercle bacilli are usually abundantly present in sputum

Symptoms

These consisting of cough expectoration weight loss fever etc usually appear late They are mild in the beginning but gradually increase as the disease progresses Pulmonary hemorrhage which occurs in about 30% of cases may be the first symptom which brings the individual to the physician

When lesions of chronic clinical pulmonary tuberculosis can first be located abnormal *physical signs* are almost never present except *in the occasional* case in whom slight splinting of the diaphragm is observed As the disease advances physical signs depend upon underlying pathology such as atelectasis consolidation and cavitation

The percussion note as well as tactile and vocal fremitus change with the underlying condition *A dull* note may be elicited over areas of considerable infiltration located near the periphery over areas of consolidation located more centrally and over thin layers of pleural fluid The note becomes flat when consolidation extends to the periphery and when a thick layer of pleural fluid is present

Bronchovesicular breathing may be heard over areas of infiltration near the periphery and bronchial breathing over areas of consolidation Breath sounds are absent over large areas of atelectasis and distant to absent over pleural fluid depending upon its thickness Bronchophony may be heard over areas of consolidation Whispered pectoriloquy and egophony suggest cavitation Post tussic rales may be heard Failure to elicit rales by no means indicates absence of pulmonary lesions

The *x ray* film is one of our best aids in diagnosis It often provides information which *is impossible to obtain from any other phase* of the examination It detects the location of lesions earlier after they attain macroscopical proportions than any other phase of the examination The x ray film often enables one to visualize changes *in* size of *lesions* and within the areas of disease such as the appearance of cavitation following evacuation of necrotic tissue before any other procedure is of avail These advantages of the x ray film justify its high position in our diagnostic armamentarium

Along with its values the diagnostician needs to know limitations of the x ray film A shadow is not sufficient in itself to justify etiological diagnosis of any disease Even pathologists who hold diseased tissue and organs *in their hands* so they can palpate them and look directly at their exterior as well as their cut surfaces cannot diagnose etiology *without the* use of the microscope culture animal inoculation and sometimes *chemical analyses*

Other limitations of the x ray film are (1) On the usual postero anterior exposure of the *single film only 75% of the lungs is* visualized The remainder is obscured from view by shadows of other organs such is the diaphragm and heart (2) The x ray film is viewed with the unaided eye therefore lesions must be macroscopical in size before they cast visible shadows Moreover macro*scopical lesions may not be sufficiently dense* to obstruct x ray so they cast no visible shadow on the film X ray inspection is of value only in a positive way—that is when it reveals an abnormality The lack of shadow on an x ray film does not denote absence of pulmonary disease



Fig 9 *From roentgenogram of the chest* of a man of 52 years Note evidence of extensive pulmonary disease First and only symptom was profuse *pulmonary hemorrhage Tubercle bacilli found* in sputum (From Myers Boynton and Diehl *Journal Lancet* April 1937)

Pathologists early discovered at postmortem examination many lesions both tuberculous and nontuberculous that had been brought well under control Many of them had not been *known to exist prior to* death nor did they contribute in any way to the exit of persons in whose bodies they were found

When x ray film inspection is made of the chests of apparently normal persons for in

surance purposes mass surveys and the like from the shadows found one has no way of knowing how long the lesions have been present or whether they are evolving or receding or if the etiological agent is malignant cells fungi pneumococci tubercle bacilli etc It first becomes necessary to determine which shadows represent tuberculous lesions and next their status *Do the shadows represent* lesions which nature has long ago controlled or recent ones now well arrested and stabilized or active lesions in the sense that they are receding or progressing? Such determinations may require weeks or months of most detailed examination and observation However nothing is more important in the entire *management of the disease*

The word "activity" is defined as the state of action or the quality of being active Obviously nothing of this nature can be seen by a single inspection of an x ray shadow which is static To make a statement with reference to activity of a lesion on x ray shadow alone some change in its size or nature must be observed This cannot possibly be done except when one inspects shadows of the same lesion at different times Hence the importance of periodical films

When lesions develop in the trachea or bronchial tree or those in adjacent lymph nodes erode into the lumina of these parts only the *bronchoscopist* can locate them One occasionally sees the individual who reacts to tuberculin but has no shadow casting pulmonary disease yet tubercle bacilli are recovered from the sputum and the bronchoscopist finds lesions in the air passages Usually it is only the bronchoscopist who can accurately discover the cause of pulmonary atelectasis due to tuberculosis and other conditions To visualize a lesion through the bronchoscope is not always sufficient but tissue or discharges procured from it by the bronchoscopist may lead to accurate diagnosis by microscopical inspection or animal inoculation

The *erythrocyte sedimentation rate* may be slightly increased but is often normal when lesions are first detectable by the x ray shadows they cast However as the disease progresses the rate is usually accelerated

There is no *sputum* to examine from early minimal lesions but stomach or bronchial washings may be searched for *tubercle bacilli* Even this is often unrevealing However as the areas of disease evolve bacilli are more likely to be found in this manner Material eliminated from the lesions is so scant as to cause no cough reflex This finds its way into *the main bronchus and then to the pharynx* when it is swallowed In the majority of advanced active cases tubercle bacilli are present in sputum

Acid fast bacilli found by *microscopical inspection* and culture and of proved pathogenicity by animal inoculation are pathognomonic Microscopical inspection of sus*pected material is only of value in a positive* way Failure to find tubercle bacille does not prove their absence In such instances numerous and frequent inspections are necessary On the other hand a single report of the presence of acid fast bacilli should not be accepted as final because laboratory errors occur with considerable frequency From microscopical inspection alone one should never report the presence of tubercle bacilli Because of the prevalence of saprophytes which appear similar to tubercle bacilli one can only state that acid fast bacilli are seen For this reason the identity and pathogenicity of acid fast organisms should be determined by culture and animal inoculation

Treatment

Although a considerable number of small chronic tuberculous lesions recede leaving only evidence of fibrous tissue (rarely calcification) the majority progress continuously or intermittently There is no way to determine when they are first seen which lesions will recede and since they are in the minority all should be treated Since as many as 25 have been observed to recede this has to be taken into consideration when any method of treatment is employed If good treatment results are not observed in more than 25 the method probably is doing no more than nature alone would have done

For minimal chronic lesions various methods of treatment have been employed from none to well regulated living to strict bed rest



Fig 10 From roentgenogram taken in November 1941 of the chest of a man of 21 years The shadow-casting lesion in the right upper lung field proved to be tuberculous Tubercle bacilli were recovered from gastric washings Two years before he reacted to tuberculin which was the first time he was tested Then and 1 year later x ray films of his chest were clear (From Myers *Tuberculosis Every Physicians Problem*)

Partial artificial pneumothorax, with an initial period of approximately 3 months or longer of strict bed rest, and continuation of the collapse for 1 to 3 years has been extensively practiced throughout the world Many have been treated by artificial pneumothorax without bed rest There are thousands of persons, living and apparently well, whose tuberculosis was long ago successfully treated by this method (Figs 10, 11 and 12)

During the last few years resection of minimal lesions under the protection of antituberculosis drugs has been strongly recommended and rather extensively practiced This method has not been employed sufficiently long to justify conclusions relative to its value when compared with artificial pneumothorax Tuberculosis is a lifetime disease and long periods of observation are necessary following any form of treatment for accruement of evidence to justify conclusions A period of 5 or 10 years is too short to learn whether more reactivations and new lesions develop in one group than in the other In the meantime, numerous experienced physicians agree with Toerning who says it is too early to determine the true value of pulmonary resections He emphasized that it is impossible to compare results from resections made under the protection of modern drug treatment with



Fig 11 From roentgenogram taken in May 1941 of same chest as seen in Figure 10. Area of disease in right lung is now well collapsed by artificial pneumothorax. This was continued for about three years. (From Myers: *Tuberculosis: Every Physician's Problem.*)

the results of artificial pneumothorax before drug treatment was introduced. The complications which occur in artificial pneumothorax are strongly influenced by the new drugs now in use and therefore these drugs should improve the ultimate results of this form of treatment to well beyond the usual 80%. He points out that in the past when properly used even without drug treatment it resulted in a lasting effect in some 80% of patients. "No other method conservative or surgical has been proved to yield more."

It must be repeated that many pulmonary lesions of the reinfection type are brought under control by the unaided defense mechanism of the body. This may be true of as many as 25%. These lesions for the most part were formerly detected at necropsy. Now they are frequently found by examining apparently healthy persons. When such lesions are detected during life, however, they are indistinguishable from those which may progress so as to cause incapacity or terminate fatally. This fact makes the evaluation of various methods of treatment difficult.

Treatment of *advanced tuberculosis* is usually complicated by *contagion* in that all contacts, including members of the family and other visitors, as well as hospital personnel, must be protected against the patient's tuber



Fig 12 From a roentgenogram taken in 1947 ... nall shadow within the circle of the first rib is interp... of clinical disease to 1957 (From Myers *Tubercul*...

cle bacilli Fortunately satisfactory contagious disease technique has been developed which if carried out painstakingly is adequate

Strict *bed rest* should be instituted in a hospital or a sanatorium where every care can be given to insure comfort dietary needs etc

Antituberculosis drugs are indicated in practically every case Those of first choice are streptomycin (SM) (dihydrostreptomycin is the hydrogenated derivative of streptomycin) para aminosalicylic acid (PAS) and isoniazid (INH) Except for the complicated or especially serious case 1 gm of streptomycin is administered intramuscularly every three days 12 gm of aminosalicylic acid in three or four equal doses by mouth daily and 5 to 8 mg of isoniazid per kg of body weight in three or four equal doses per day by mouth are now thought to be satisfactory doses (For the average size person 300 mg of isoniazid daily is usually prescribed) Any two of these drugs should be administered simultaneously since in combination they have a better effect than either one alone This leaves a major drug in reserve in the event it becomes necessary to substitute it for one being administered The combination of para aminosalicylic acid and isoniazid is slightly better than any other Moreover they have the advantage of being administered orally

While no fixed rule can be established for



Fig 13 F... ulmonary tuber... 1923 was given ... in the left side ... After a period of ... has continued without interruption to the present time (From Myers Tuberculosis *Every Physicians Problem*)

all cases it is now generally thought that drugs should be continued for at least a year in all cases 18 months to 2 years in some and even indefinitely in a few A fact of great importance is that antituberculosis drugs do not eliminate all tubercle bacilli from the bodies of persons with chronic tuberculosis However they do have a good suppressive effect on bacilli in well vascularized lesions Thus most fresh progressive areas of disease show evidence of recession within a few weeks or months However the avascular necrotic areas in which tubercle bacilli have not been reached remain unchanged

Other drugs than those mentioned which have been found useful are (1) viomycin (VM) It is not as effective as the major drugs but is sometimes substituted when organisms have become resistant etc to another drug It is best administered in doses of 2 gm a day twice a week that is 1 gm morning and evening to be repeated about three days later It is not given daily because of its toxicity



Fig 14 From a roentgenogram taken January 1953 of the chest of a man of 31 years The shadow casting d sease in the right upper lung field proved to be tuberculous Tubercle bacill were recovered from the sputum After an adequate course of antituberculosis drugs the area of disease was resected (From Myers *Tuberculosis Every Physicians Problem*)

Terramycin is sometimes used in combination with streptomycin or isoniazid if para aminosalicylic acid is not well tolerated However this drug alone has limited bacteriostatic qualities

Pyrazinamide (PZA) is administered in combination with isoniazid with considerable effectiveness The dose is 2 to 3 gm daily

Cycloserine (Seromycin) a relatively new drug administered orally in a dose of 1 to $1^1/_2$ gm per day in divided doses has been found of considerable value

In recent years there has been a tendency to administer *artificial pneumothorax* in fewer cases of advanced tuberculosis than in the past In well selected cases however administered with antituberculosis drugs it is a good method of treating pulmonary tuberculosis

Pneumoperitoneum has a relaxing effect on pulmonary lesions resulting from elevation of the diaphragm thus reducing the excursion of both lungs It has been found more effective in lesions located proximal to the diaphragm than in those of more remote locations However good results have been reported on lesions in the upper half of the lung field Even though pneumoperitoneum does not constitute adequate treatment in many

cases it may prepare the patient for more drastic procedures such as resectional surgery which were not previously possible

Extrapleural thoracoplasty which consists of removing ribs in whatever number is necessary to allow the chest wall to collapse on and with pulmonary disease has been extensively employed and served a valuable purpose during the greater part of this century However because of such factors as thickness of walls in 30% or more cavities were changed in shape but were not completely obliterated Thus the sputum was not converted and isolation was still necessary Despite its usefulness as manifested by the large number of persons who have lived practical normal lives following thoracoplasty (Fig 13) the number of failures to convert sputum was sufficiently large to have caused this method of treatment to be nearly abandoned in favor of resectional surgery

Such operations as phrenico exeresis and phrenemphraxis as well as most extrapleural operations have been nearly abandoned This also includes hyperthermia x ray treatment heliotherapy, tuberculin and change of climate

Pulmonary Surgery

Present day pulmonary surgery was made possible by (1) anatomists learning that pulmonary lobes are divided into segments which can be removed individually (2) antimicrobial drugs usually preventing pyogenic infections and antituberculosis drugs which markedly suppress tubercle bacilli and usually prevent significant spread of these organisms (3) liberal use of blood so that lost during surgery is mainly replaced (4) new developments and expertness of anesthesiologists and (5) new surgical techniques

In some institutions surgical removal of residual lesions is recommended when the "target point is reached This consists of (1) the disease has become stable (2) conversion of sputum and (3) cavities apparently have closed Removal of large areas of fibrocaseous disease contracted lobes thick walled cavities etc which in the past were usually not well controlled by other methods has contributed significantly to the advancement of treatment of pulmonary tuberculosis (Figs 14 and 15)

As yet there is no method of treating pulmonary tuberculosis including resectional surgery which effects a cure of the disease Although demonstrable lesions are removed often to the great benefit of the patient there are always numerous other lesions left behind not only in the lungs but in extrathoracic organs which are harboring viable tubercle bacilli Although they are causing no present illness one or more of them at any time may become clinical and require treatment Therefore it is important that each person who has a diseased lung lobe or segments removed be thoroughly informed that he still has a tuberculosis problem Many catastrophies have occurred because people who have made good recoveries from clinical lesions have assumed that they were cured from tuberculosis

Complications

Pulmonary *hemorrhage* which may occur at any time during the course of treatment is probably the most frightening *complication* to the patient This is rarely fatal but death may result from aspiration of blood into the bronchial tree so as to cause "drowning" or asphyxiation Aspirated blood may lead to pneumonia In some cases blood and the surrounding reaction casts x ray shadows for a considerable time which may be erroneously interpreted as extension of disease In addition to strict bed rest mild sedatives such as bromide or phenobarbital usually relax enough to allay fear and promote sleep Morphine or other narcotics should never be used to the point of abolishing the cough reflex Usually hemorrhages come under control without drastic measures but occasionally if loss of blood is large or the bleeding persists artificial pneumothorax may be employed and in rare cases pulmonary resection may be indicated

Since the lungs contain no sensory pain nerve fibers *pain* in the chest is not from the lungs Usually it is caused by pleural involvement Tuberculous laryngitis and enteritis may be exceedingly painful Sedatives are indicated and if excruciating pain per



Fig 15 Made from roentgenogram of chest taken July 1954 of the same man shown in Figure 14 (From Myers *Tuberculosis Every Physicians Problem*)

sists even narcotics in small doses may be used for brief periods

Tracheo bronchial lesions often complicate pulmonary tuberculosis Insofar as possible they should be located by bronchoscopy Bronchoscopists are often able to remove material causing partial or complete obstruction from bronchial ramifications and relieve localized emphysema or atelectasis These lesions usually respond promptly to anti tuberculosis drugs

Extrathoracic tuberculous complications including lesions in bones joints urogenital tract gastro intestinal tract larynx and pharynx should be treated promptly

diagnosis Most of them respond to anti tuberculosis drugs

Several *nontuberculous pulmonary complications* may tend to interfere with treatment of the tuberculous disease such as pneumonia and abscess They should be treated in the same manner as in nontuberculous persons When primary malignancy is found sufficiently early it should be treated by extirpation provided the patient s general condition permits and enough good lung tissue remains to provide adequate respiratory function This also applies to bronchiectasis of limited extent which may be interfering with recovery

Silico tuberculosis has probably been over

estimated from the standpoint of prevalence, severity and response to treatment It is impossible to differentiate by x ray shadows *alone between the silicotic and the tuberculous* components However the tuberculin reaction may lead one to suspect clinical tuberculosis Only a small percentage of people with silicosis develop clinical tuberculosis When the silicotic individual reacts to tuberculin tubercle bacilli should be sought in sputum or in stomach washings There is no known treatment for silicosis but the tuberculous lesions should be treated with antituberculosis drugs and other measures in the usual way

Nontuberculous extrapulmonary complications should usually be treated in the regular manner For example, foci of infection in the upper respiratory tract in the appendix or anywhere else may be treated or removed often aiding in the control of the pulmonary lesion

Formerly about 16 times more diabetic children and about 4 times more diabetic adults developed clinical tuberculosis than non diabetics Every person with diabetes regardless of age should be checked carefully for tuberculosis and vice versa Tuberculosis in the presence of untreated and uncontrolled *diabetes usually is difficult to treat success*fully However if the diabetes is brought under control and kept so most tuberculous *lesions* respond to treatment in the same manner as those in non diabetics

Mental aberrations often seriously complicate the treatment of pulmonary tuberculosis Lack of cooperation in carrying out routine measures make some forms of treatment almost futile Among those who are hospitalized important steps have been taken in recent years consisting of screening all mentally ill persons and isolating those found to have clinical tuberculosis When they are assembled in one or a few *places* the volume of work is sufficient to procure expert nursing and medical service including all aspects of diagnosis *and treatment conducted under* rigid contagious disease technique Antituberculosis drugs are freely administered and *resectional surgery is done as indicated* Lewis et al have reported on the surgical treatment of the 100 tuberculous mentally ill who have been assembled in a special tuberculosis unit in one state institution These procedures have resulted in conversion of *sputum in many cases* thus facilitating the subsequent care of the patients with reference to contagion and also salvaging those whose *mental condition* can be successfully treated

Pregnancy was formerly thought to be a serious complication However more careful study and prolonged periods of observation have revealed that it has little if any deleterious effect on tuberculosis and therefore tuberculous pregnant women with rare *exceptions* now have their tuberculosis treated with approximately the same results as others

Direct *injury* to a well controlled tuberculous lesion so as to liberate tubercle bacilli can result in fresh clinical disease in the vicinity Otherwise *trauma* plays little or no role as a complication

Contrary to a long held belief there is no innate difference in the response to tuberculosis among the *races of people* When identical social and intellectual conditions exist lesions of the American Indian and Negro respond to treatment in the same way as those of Caucasians

Even elderly people (40 *years and older*) may now have pulmonary tuberculosis controlled by the same effective methods as are employed in the earlier decades of *life*

Rehabilitation and Follow up

During and after treatment it is important to rehabilitate and follow the patient When an individual's pulmonary lesions have been treated adequately and he is restored to society with good working capacity he still needs a physician who must understand that the tuberculosis is not cured that he may need treatment again and again for progressive lesions which may *subsequently* evolve in his lungs or elsewhere throughout the remainder of his span of life The fact that tuberculosis is a lifetime disease cannot be re-emphasized too often or too strongly This person should not be alarmed but should be told of these possibilities with emphasis on the fact that if he is kept under surveillance with sufficiently frequent periodic examinations present le-



Fig 15 Made from roentgenogram of chest taken July 1954 of the same man shown in Fig 14 (From Myers *Tuberculosis Every Physicians Problem*)

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of little or no value Indeed anachronisms now in vogue are consuming time and energy of thousands of workers and costing millions of dollars without benefit to the tuberculosis eradication program For example much time and energy are wasted in arguments and controversy as to the different effects tubercle bacilli might have as they enter human bodies at different ages of life Opinions speculations and theories are rife but well documented evidence is lacking to show that age makes any difference whatsoever

The literature abounds with statements to the effect that people of different races and nationalities are more susceptible to infection and resist tubercle bacilli more poorly than others For example American Indians and Negroes have often been referred to as primitive races with little or no resistance to tubercle bacilli At the opposite extreme Jews are said to be most resistant of all the peoples of the world These erroneous deductions were derived from facts For example it was long observed that morbidity and mortality rates were exceedingly high among American Indians and Negroes but relatively low among Jews Little or no consideration was given to differences in social hygienic conditions and care provided for Indians and Negroes as contrasted with that among Jews dating to the health measures taught by Moses Wherever Indians and Negroes have had the same social conditions and the same health measures they have resisted tubercle bacilli and responded to treatment in the same manner as their Caucasian brethren There is no question about the facts being correct with reference to the destructiveness of the disease among Indians and Negroes but the deductions were wrong with reference to cause

This also applies to persons suffering from mental illness who only a few decades ago were said to have high susceptibility and low resistance to tubercle bacilli because of the mental condition Accurate observations however have shown that the high tuberculosis rates which obtained in institutions for the mentally ill were due to contagion which was permitted to exist rather than the mental illness

The theory that initial tuberculous infection postponed to adulthood is a much more serious condition than when acquired in childhood is no longer tenable

The belief that clinical disease usually develops within 2 years after initial infection with tubercle bacilli was largely due to failure to differentiate primary pulmonary infiltrates from reinfection clinical type of disease Longitudinal observations of persons first infected in childhood or adulthood have thoroughly disproved this concept In fact there is good evidence that most of the morbidity and mortality are now occurring in the United States and some other parts of the world as the result of infections acquired long ago

A belief is extant to the effect that most persons whose lesions reactivate or who have new ones appear do so within 2 years after apparently successful treatment Here again longitudinal observations have proved this belief to be a fallacy

Even bitter controversies have been waged concerning portals of entry One school has clung tenaciously to the belief that most pulmonary tuberculosis is the result of tubercle bacilli entering through the respiratory tract while another school speaks just as loudly for the digestive tract Evidently the portal of entry makes no difference since it is well known experimentally that when tubercle bacilli are introduced directly into the intestines subcutaneously intracutaneously intrapleurally or the blood stream they may soon be found in the lungs just as surely as when introduced directly into the respiratory tract The point of importance is that they are allowed to enter the body by any portal

Since Hippocrates time there has been a widely accepted belief that certain foods provide resistance against tubercle bacilli Practically every food element has been employed singly and in combination but throughout thousands of years no one has shown incontrovertibly that food beyond the daily requirement plays a role in resisting tubercle bacilli Moreover persons with the best known nutrition become infected with tubercle bacilli when invaded by them

The numerous attempts to build resistance to tubercle bacilli by introducing living or

sions that may evolve to clinical proportions can usually be detected before they have caused much destruction of tissue and when they can be treated successfully The presently restored individual has succeeded in just one skirmish While this may be the last he and his physician must face the possibility of others

Acute exudative lesions may occur almost overnight These have been observed while persons are on strict bed rest and the lesions for which treatment was instituted were showing improvement

Persons who have had what is considered *adequate treatment with no change in x ray* film shadows over long periods may have sizeable areas of necrotic tissue suddenly discharge into bronchial ramifications, after which the x-ray film reveals evidence of cavitation These may appear during hospital or sanatorium periods or at any subsequent time

Prognosis

In minimal chronic pulmonary tuberculosis, adequately treated, prognosis is excellent It was exceedingly good in the pre-antituberculosis drug days When lesions are seen soon after they begin to cast x-ray shadows, well nigh all can be treated successfully In the occasional case, however, with the best treatment known, tuberculosis may not come under control and new lesions may evolve while treatment is being administered

Much depends upon the patient himself If he cannot be made to understand the seriousness of the situation, does not follow the advice of his physician and nurses with reference to the various recommended procedures, throws prescribed drugs out the window or in the toilet, leaves against medical advice on the initial admission or re admissions, in general the ultimate *prognosis is bad*, regardless of the stage of disease at the beginning of treatment

Many physicians remember when approximately 40% of tuberculous patients died within a few years and as many as 80% within 10 years after the original diagnosis This was partly because so many did not report for examination or facilities were not available to them until they were ill and often, desperately so

Even now, it is a serious reflection on the medical profession in particular and all health workers in general that 78% of the new cases of tuberculosis reported in the United States in 1955 had advanced disease This situation has obtained almost without improvement for many years

From available evidence, it is believed that prognosis in tuberculosis is not now one-half as bad as it was in former years. *When the best known treatment is administered and is continuously accepted by patients and the disease is not too extensive at the beginning, the majority of patients remain free from symptoms, have no recoverable tubercle bacilli, no change* in lesions as manifested by x ray shadows, and are working full-time a few years after discharge from institutions. This is a brief time in tuberculosis since it is a lifetime disease

An important fact is that individuals successfully *treated have other lesions which may* later evolve in the lungs or elsewhere Therefore, all persons who have overcome one bout of clinical tuberculosis should be kept under surveillance

Prevention

The only known way to prevent chronic clinical pulmonary tuberculosis, like all other forms of the disease, is avoidance of the initial invasion which leads to primary tuberculosis *which in turn leads to all of reinfection* clinical forms No special diet or preservation of energy beyond that included in well regulated living has been found to prevent evolution of chronic clinical pulmonary tuberculosis *Advanced disease can usually be prevented by periodically examining adult tuberculin reactors so as to find lesions in the minimal stage and treating them adequately*

PHYSICIANS' ROLE IN TUBERCULOSIS *ERADICATION*

Anachronisms now constitute the most serious handicap to the eradication of tuberculosis This term applies to teachings and practices originally based on theories and opinions which have long been in use *but have proved*

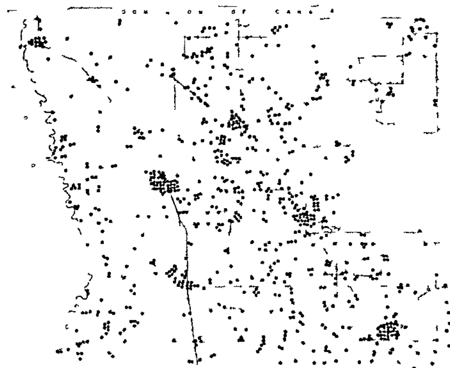


Fig 16 Map of Kittson County Minnesota (1954) Dots indicate persons harboring tubercle bacilli as manifested by the tuberculin reaction This is a so-called low incidence tuberculosis area since only one person died in the county and only three new clinical cases were reported that year In reality there were 2 100 persons who had tuberculous lesions harboring tubercule bacilli as manifested by the tuberculin reaction (From Myers *Dis Chest* July 1956)

fidence of the citizenry It impresses upon all the people the fact that local physicians are capable of doing modern tuberculosis work Moreover it squelches those who believe and teach that physicians are interested only in fees

Such projects are not without precedent Indeed in 1941 the physicians of Meeker County Minnesota voted unanimously to conduct a county wide tuberculosis control program without financial remuneration They found that approximately 23% of the citizens had at least microscopical lesions harboring tubercle bacilli Moreover they learned just where the tubercle bacilli of their county were located Continuing with the examination of the tuberculin reactors they found 16 persons in whom tuberculosis had evolved to such gross proportions as to be detectable by x ray film inspection of the chest

These physicians realized that among the tuberculin reactors whose x ray films were clear at the moment some lesions would evolve to shadow casting size Therefore all such reactors should subsequently be examined periodically They also realized that some persons who did not react to tuberculin would subsequently become infected and therefore all nonreactors must be retested periodically When the demonstration was over work of physicians was no longer on a gratis basis but the usual fees for administering tuberculin tests making x ray film inspection of the chest etc were charged Since the demonstration proved to the citizenry that periodic examinations for tuberculosis are desirable many more persons have been examined periodically by private physicians than would have reported to them had the survey not been conducted Thus the demonstration survey constituted a long step toward eradication of the tubercle bacilli in that county

dead organisms have been unavailing No one has yet proved indisputably that *efficaciousness* of the tubercle bacilli resisting mechanism with which each human body is endowed has been aided by special nutrition or administration of living or dead organisms

The first project of the medical profession everywhere should consist of abandoning *anachronisms and employing those methods that strike at the heart of tuberculosis* namely the tubercle bacilli The attack must be an offensive not a defensive one

There is no more important project for the medical profession than early case finding *whether it be in physicians offices clinics* hospitals surveys or elsewhere that affords opportunity for examinations The person who reacts characteristically to tuberculin has at least microscopical lesions harboring tubercle bacilli Such lesions can be detected by the tuberculin reaction within three to seven weeks after invasion of tubercle bacilli occurs *Therefore this is by far our earliest* diagnostic method

Although x ray shadows of lesions are never pathognomonic lesions which prove to be tuberculous occur only among persons who *react to tuberculin* Chronic lesions which evolve in the lungs usually can be found by the shadows they cast long before symptoms or physical signs are present Therefore the x ray film is not the method which detects tuberculosis earliest but is the method which detects evolving gross lesions earlier than any other procedure Finding shadow casting lesions in a tuberculin reactor necessitates bacteriological study and sometimes biopsy The fact of great importance is that a tuberculin reactor in the absence of all other findings is a case of tuberculosis The only difference between such an individual and one who is dying from the disease is one of evolution of lesions

Another important project following the diagnosis is to provide for adequate treatment which obviously depends upon the stage of the disease *The contagious case must immediately* be isolated so as to prevent the spread of tubercle bacilli among persons including hospital and sanatorium personnel Technique is now available for this purpose

The divergence between morbidity and *mortality graphs* in most parts of the world since 1947 has resulted in confusing statements This situation is not a mysterious phenomenon but rather one with a clear explanation In places where offensive attacks on *tubercle bacilli have been in progress for* a few decades the infection attack rate has been decreasing along with and parallel to morbidity and mortality rates Since 1947 infection attack and morbidity rates have continued to decrease as previously However anti tuberculosis drugs have at least postponed many deaths and thus the mortality graph *decreased rapidly Hence the divergence between* morbidity and mortality rates The faster the medical profession and its allies decrease the infection attack rate the faster the morbidity rate will decline as these two phases of the disease run parallel courses

A popular movement now under way consists of offering examination to persons of all ages in an entire community county or even larger areas This is a cooperative activity with the medical profession local and state boards of health along with local and state tuberculosis and health associations Physi*cians must make the examinations* boards of health serve as official agencies and tuberculosis and health associations provide such phases as education *activities procedures etc*

Examination consists of first offering the tuberculin test to every citizen regardless of age Reactors have x ray film inspection of the chest and those with shadow casting lesions have complete examinations to determine etiology Isolation and treatment are instituted when indicated Extra thoracic *tuberculous lesions such as those of bones* joints superficial lymph nodes and kidneys must also be given consideration Physicians who participate in such projects without *immediate* financial gain render a service to their communities which no other individual can do Moreover tuberculosis is the problem of the physician and his family just as it is of everyone else in the community Therefore in demonstration projects the physician should give of his time as freely as is done by other citizens *This public service* on the part of the medical profession increases con

A project of proved value consists of preparing a *spot map* following a tuberculin testing survey, showing just where tuberculin reactors have been found Such a map was produced in a country of so called low tuberculosis incidence In fact, only one person died from tuberculosis in that county the previous year and only three clinical cases were reported However, this map (Fig 16) reveals that 2,100 persons, mostly elderly people, are harboring tubercle bacilli, each of whom is a potential case of clinical tuberculosis If cognizance is not taken of this problem and clinical cases are not found as they evolve among the tuberculin reactors, they can soon disseminate enough tubercle bacilli to create a tuberculosis problem as serious as when the Twentieth Century began

The Committee on Tuberculosis of the American School Health Association devised a plan whereby individual or whole systems of schools are officially *certified* on the basis of tuberculosis control work in progress In order to be awarded a first class certificate, at least 95% of the children from kindergarten through high school and 100% of the personnel, must have x ray film inspection of the chest, and those with shadow casting lesions completely examined When these qualifications are met, the official certificate (Fig 17) is issued by the American School Health Association and the Local or State Tuberculosis and Health Association

This project is in vogue in several states, and thousands of certificates are displayed on the walls of schools This program spells the doom of the tuberculous bus driver, engineer, janitor, teacher, other employee and even high school students from spreading tubercle bacilli to other personnel and students The success of this project depends upon the cooperation of the local medical profession

In most parts of this country mass chest x ray surveys are not economically sound In many places they are being abandoned and replaced by x ray surveys of certain groups such as elderly persons prisoners inmates of institutions for the mentally ill and hospital admissions It has already been shown that this is not good economy The only sound and effective method consists of screening from an entire population or any special group those who now or later are found to harbor tubercle bacilli by the tuberculin reaction and concentrate subsequent effort on them

A belief is extant to the effect that all gross clinical cases of tuberculosis that will occur could now be found if x-ray film inspection were made of everyone's chest Unfortunately, the situation is not so simple If the estimated 55,000,000 tuberculin reactors in this country promptly had x ray film inspections of their chests, it is likely that only 1% or less would present evidence of significant lesions Sight is often lost of the fact that new clinical lesions evolve among reactors from year to year throughout the remainder of their lives regardless of their present ages Little would be accomplished if only the relatively few reactors with present gross lesions were found and properly managed and the crop of clinical and contagious lesions which will evolve among the remaining 99% is not harvested as it matures This problem can be solved only by periodical examinations throughout the lives of those who react to tuberculin but whose x ray films of the chest are now clear

THE GOAL

The ultimate goal is eradication of tubercle bacilli Unless some method of destroying these organisms in avascular lesions is devised, their eradication will be accomplished only by keeping them corralled in the bodies of people who now possess them as long as these individuals live Thus, if from this moment no more new infections occurred, eradication is as far away in point of time as the death of the last person now harboring tubercle bacilli It is true in this country that the vast majority of tubercle bacilli have taken refuge in the bodies of older people who will die within the next few decades With their passing there will remain the relatively few infected persons who are now younger but in whose bodies bacilli must be kept corralled for the remainder of their lives

Infants infected today may remain in good health through long lives but still may become clinical and contagious cases of tuberculosis in senility from progeny of tubercle bacilli

Tuberculosis Control Award

American School Health Association

and

State Tuberculosis and Health Association



This is to certify that

OTTUMWA HIGH SCHOOL

has fulfilled the minimum requirements of the American School Health Association for the control of tuberculosis, in consideration for which a Class A Certificate is granted

Paul C. Williamson — Executive Director State Tuberculosis Association

C. W. Gray, M.D. — State Subcommittee Chairman

President A S H A

A. O. DeWeese M.D. — Secretary A S H A

Fig 17 Certificate awarded Ottumwa High School, Iowa, in 1956 Several thousand similar certificates are now exhibited by schools in various states They were officially granted schools on the basis of tuberculosis control work in progress by the American School Health Association and state tuberculosis and health associations (From Myers *Tuberculosis Every Physician's Problem*)

Subsequently, the citizenry of several counties and municipalities have conducted similar demonstrations with approximately the same results as reported for Meeker County In the city of Hastings, Minnesota, with a population of 6,200, 90% responded The tuberculin test was administered gratis by local physicians and x ray films of reactors were exposed, developed and read at cost

In St Louis Missouri, the Academy of General Practice adopted a tuberculin testing program in the schools in 1951 as a public service To date, 200 000 children have received tests Examinations have been completed as indicated and sources of children's infections have been sought with success This service has resulted in increased confidence of the public in the physicians in general practice

It is not a question of whether physicians can afford this service gratis, but rather, that they cannot afford to overlook such an opportunity It is an excellent way of securing and maintaining confidence, good will and support of citizens These are the factors which are so needed in returning the proper part of the tuberculosis problem to the offices of physicians, particularly those in general practice As this is accomplished, we should experience the most effective attack of all time upon the tubercle bacillus

Veterinarians and their co workers found that by providing counties with *official certificates* after meeting certain control qualifications, widespread interest and increased activity in eradication work was created Accreditation of counties on the basis of accomplishments in tuberculosis control among humans has been demonstrated to be of great value by insuring participation of physicians as well as the entire citizenry in the tuberculosis eradication movement

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Tuberculosis Control Award

American School Health Association

and

State Tuberculosis and Health Association



This is to certify that

OTTUMWA HIGH SCHOOL

has fulfilled the minimum requirements of the American School Health Association for the control of tuberculosis, in consideration for which a Class A Certificate is granted

Paul C. Williamson
Executive Director State Tuberculosis Association

President A S H A

C. W. Gray, M.D.
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Subsequently the citizenry of several counties and municipalities have conducted similar demonstrations with approximately the same results as reported for Meeker County In the city of Hastings Minnesota with a population of 6 200 90% responded The tuberculin test was administered gratis by local physicians and x ray films of reactors were exposed developed and read at cost

In St Louis Missouri the Academy of General Practice adopted a tuberculin testing program in the schools in 1951 as a public service To date 200 000 children have received tests Examinations have been completed as indicated and sources of children s infections have been sought with success This service has resulted in increased confidence of the public in the physicians in general practice

It is not a question of whether physicians can afford this service gratis but rather that they cannot afford to overlook such an opportunity It is an excellent way of securing and maintaining confidence good will and support of citizens These are the factors which are so needed in returning the proper part of the tuberculosis problem to the offices of physicians particularly those in general practice As this is accomplished we should experience the most effective attack of all time upon the tubercle bacillus

Veterinarians and their co workers found that by providing counties with *official certificates* after meeting certain control qualifications widespread interest and increased activity in eradication work was created Accreditation of counties on the basis of accomplishments in tuberculosis control among humans has been demonstrated to be of great value by insuring participation of physicians as well as the entire citizenry in the tuberculosis eradication movement

A project of proved value consists of preparing a *spot map* following a tuberculin testing survey showing just where tuberculin reactors have been found Such a map was produced in a country of so-called low tuberculosis incidence In fact only one person died from tuberculosis in that county the previous year and only three clinical cases were reported However this map (Fig 16) reveals that 2 100 persons mostly elderly people are harboring tubercle bacilli each of whom is a potential case of clinical tuberculosis If cognizance is not taken of this problem and clinical cases are not found as they evolve among the tuberculin reactors they can soon disseminate enough tubercle bacilli to create a tuberculosis problem as serious as when the Twentieth Century began

The Committee on Tuberculosis of the American School Health Association devised a plan whereby individual or whole systems of schools are officially *certified* on the basis of tuberculosis control work in progress In order to be awarded a first-class certificate at least 95% of the children from kindergarten through high school and 100% of the personnel, must have x ray film inspection of the chest and those with shadow casting lesions completely examined When these qualifications are met, the official certificate (Fig 17) is issued by the American School Health Association and the Local or State Tuberculosis and Health Association

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which invade their tissues today Thus, if infants are infected now, the tuberculosis eradication goal is no nearer than it was when this century began

Eradication of tubercle bacilli *must apply* to the three now known pathogenic types—human, bovine, and avian Each of them produces clinical disease in more than one species of animals and all cause such disease in people It is of little avail *to eradicate the* human type with the others extant and vice versa Therefore, it is important that the *medical* profession cooperate with the veterinary medical profession in the all out eradication movement

Although veterinarians and their allies are approaching the bovine eradication goal and have *attained it in many places, they continue* to tuberculin test the entire cattle population of this country periodically A G Karlson, D V M, Mayo Foundation, says "An animal that reacts positively to the tuberculin test is properly considered as a dangerous individual in spite of the great advances in control, there is a constant potential hazard as long as *only a few infected animals exist*" This statement is equally true of people

We must agree with David T Smith, Duke University, when he says that even in this country where so much has been accomplished, we have not even reached the half way mark in our eradication program The more difficult and laborious work remains to be done *Any tuberculosis association that* sets eradication as its goal and is willing to do the necessary work will have plenty to do throughout the lifetime of every person now engaged in the work Much will remain to be done by our successors

Just as we strove through the decades of this century to drive downward the mortality rate from nearly *200* and *the morbidity rate* from 2 000 per 100,000, we must now strive to drive downward the case rate of approximately 30,000 per 100 000 population Our future success must be measured in reductions of this real case rate, and the goal will not be reached in any community or state until there is no case of tuberculosis manifested by the tuberculin *reaction*

There is no shortcut to the tuberculosis eradication goal Every person who is now infected must be examined periodically as long as he lives or as long as he harbors tubercle bacilli This applies to all who *henceforth become infected* Many persons now harboring tubercle bacilli will be living when the Twenty-first Century opens Therefore, if all infections were stopped today, the disease could not possibly be eradicated during *this century However, if all persons now* infected were kept under adequate observation, the eradication goal could be within shouting distance when the Twenty-first Century begins

We must gird for a long, strenuous fight Just as "a walking journey of a thousand miles begins with a single step," our long journey *begins with promptly putting into operation* all that we know about tuberculosis and diligently pursuing the tubercle bacillus to its last member

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CHAPTER 9

Pulmonary Mycoses

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INTRODUCTION

FOR MANY years mycotic diseases of the lungs have been regarded as rare, exotic infections which were of interest to the esoteric specialist but did not concern the average general practitioner or internist. Evidence has accumulated during the past twenty years to change this point of view. We know now that *mycotic infections occur with sufficient frequency to justify their being considered in the differential diagnosis of very difficult and complicated pulmonary and systemic infection.*

Some of the mycoses, such as moniliasis, geotrichosis and actinomycosis, are endogenous infections analogous to pneumococcus pneumonia and may occur *at any time, in any climate* and *in any strata of society.*

Other mycoses, such as coccidioidomycosis, histoplasmosis, North American blastomycosis and South American blastomycosis, have *a fairly fixed geographic distribution.*

Certain fungus infections have increased in number and severity since the introduction of the broad spectrum antibiotics, apparently as a result of a temporary destruction of the normal harmless bacterial flora which usually holds the fungus flora in check. The wide spread and often uncritical use of the corticosteroid hormones has increased the number of infections with fungi of limited pathogenicity and accelerated the dissemination of fungi with primary pathogenicity.

The infecting fungi obviously are present somewhere in nature, but whether they are primarily parasites of animals and plants or merely saprophytes in the soil has not been determined. Sporotrichosis, which is world-wide in distribution, is primarily a disease of plants, and man is an accidental and terminal host.

Coccidioidomycosis is endemic in the dry sandy areas of the entire southwestern part of the country. Positive skin tests with coccidioidin have shown that 60 to 80 per cent of the inhabitants of certain areas have been infected with *Coccidioides immitis*. Additional studies have shown that there is a benign primary form of the disease which is very prevalent in these areas. The benign form of the disease occurs by the thousands while the malignant, progressive, highly fatal form is numbered by the hundreds. Obviously *it is important in a difficult diagnostic problem to know if the patient has made a visit, even a very brief one, to the arid Southwest.*

Histoplasmosis is another mycosis with a fairly definite geographic distribution. In certain areas of the Mississippi and Ohio river valleys over 60 per cent of the population have had subclinical infections with *Histoplasma capsulatum* as demonstrated by positive skin tests to histoplasmin. The skin testing surveys by Christie, by Palmer, by Furcolow and by Loosli suggest that over 30 million persons in Central United States have been infected with this fungus. Clinical cases of histoplasmosis are now recorded by the hundreds.

North American blastomycosis may be found anywhere on the continent of North America but occurs with the greatest frequency in the Mississippi Valley, across Tennessee and down

into the Southeastern states with North Carolina as the center of the endemic area The great prevalence of this disease has been demonstrated by the work of Conant Martin Smith Baker and Callaway of Duke University

Only one epidemic of blastomycosis has been recognized and this occurred in Eastern North Carolina A skin testing and serologic survey of the population in this area showed that *asymptomatic infections with Blastomyces dermatitidis* do occur

Of all the non tuberculosis infections the *mycoses most closely resemble tuberculosis* Disease producing fungi grow slowly in the tissues they induce giant cell formation and frequently produce a state of tissue hypersensitiveness which is analogous to that occurring in tuberculosis Some of the mycoses such as geotrichosis, moniliasis and aspergillosis are relatively mild diseases but others such as North and South America blastomycosis *coccidioidomycosis cryptococcosis and* histoplasmosis have a mortality much higher than that of tuberculosis

The yeast like and mold like fungi are completely resistant to the antibiotics which are so effective in the treatment of bacterial diseases The chemotherapeutic agent hydroxystilbamidine is remarkably effective in the treatment of blastomycosis and preliminary reports suggest that the new antibiotic Amphotericin B is effective in the therapy of histoplasmosis coccidioidomycosis blastomycosis cryptococcosis and moniliasis

ACTINOMYCOSIS

Actinomycosis is the most common and the most widely distributed of the severe systemic mycoses

Recent work has shown that the patient's own mouth is the source of infection in pulmonary actinomycosis Pathogenic actinomycetes have been found in the tonsils and about the teeth of apparently normal individuals Such fungi are in a strategic position to invade the jaw locally giving rise to cervical actinomycosis to be aspirated into the lungs to initiate pulmonary infection or to be swallowed and infect the intestines and abdominal organs

Pulmonary infections with actinomycetes are usually bilateral and basal but they may occur as a unilateral lesion in any part of the lung (Fig 1)

The symptoms in the first few weeks of the disease are those of a subacute pulmonary infection with a mild irregular fever cough and some expectoration The sputum becomes mucopurulent and may contain blood as the disease progresses and small abscesses develop in the lung Sometimes the infection begins in one or more ribs invading both the lung and the subcutaneous tissues Pulmonary infections usually extend to the pleura causing



Fig 1 Pulmonary actinomycosis There is some evidence of atelectasis as well as infiltration

pleural pain An occasional patient develops a pleural effusion but the fungus more often invades directly through the pleura to the chest wall giving rise to numerous draining

sinuses As the disease progresses patients lose weight and strength and become anemic they develop spiking temperature night sweats *dyspnea and other signs* of severe pulmonary disease The infection may extend into the mediastinum causing dysphagia and at times there is an invasion of the pericardium and heart The sedimentation rate is elevated and there is an increase in the white blood count with a rise in the percentage of poly *morphonuclear leukocytes The physical signs* in the early stages resemble those of tuberculosis except that the primary site of infection is more often at the bases of the lungs As the disease progresses massive areas of dull ness appear and the chest wall may be retracted and limited in motion The presence of *subcutaneous abscesses* or open draining sinuses should suggest the possibility of mycotic infection

The *chest films* usually show smooth irregular massive areas of consolidation without cavity formation or with small irregular areas of rarefaction Although the lesions may appear in any part of the lung they are found most often in the lower lobes and are usually bilateral Sometimes areas of massive consolidation project from the hilum and have the appearance of a neoplasm In the advanced cases the pleura usually is involved with either massive pleural adhesions or massive accumu lations of fluid which may or may not be encapsulated The ribs are invaded frequently and usually show both destructive and proliferative changes

The *diagnosis* is established by finding the typical "sulfur granules or tangled masses of gram positive branching filaments in the *sputum When subcutaneous abscesses* are present pus aspirated from unopened lesions should be examined directly for the fungus and cultured under both aerobic and anaerobic conditions When open secondarily infected draining sinuses are present in the chest wall the inner layers of the gauze dressings should be examined under the low power of the microscope for the presence of "sulfur granules"

Actinomycosis presents a variety of clinical pictures and it must be differentiated from tuberculosis syphilis neoplasm tularemia osteomyelitis and staphylococcic actinophytosis (botryomycosis) as well as certain other mycoses especially North American and South American blastomycosis coccidioidomycosis cryptococcosis and sporotrichosis

The *prognosis* in pulmonary actinomycosis is grave Before the discovery of sulfonamides and penicillin only about 25 per cent of the cases of pulmonary actinomycosis recovered following medical treatment with potassium *iodide or after surgical drainage* The prognosis is much better with newer types of treatment

The patient with pulmonary actinomycosis should have the same general supportive treatment as that given a case of tuberculosis and the treatment should include in addition to a good *diet extra vitamins especially A* and D and fruit juices All of the sulfonamides have been used successfully in the treatment of pulmonary actinomycosis Sulfadiazine seems to be the drug of choice at the present time although gantricin has theoretical advantages Potassium iodine should be administered concurrently with the sulfonamide therapy The sulfonamide blood level should be maintained between 5 and 10 mg per cent The potassium iodide is administered orally using a saturated solution of the drug The usual procedure is to give 3 drops t i d p c in one half ounce of water The dose is increased either by one drop each day or 3 drops each day until the patient is receiving 20 drops t i d After reaching 20 drops t i d we have found it advisable to reduce the dose to 3 drops t i d and then gradually increase it again to the maximum of 20 drops t i d Occasionally it is necessary to give much larger *doses even up to 3 to 4 gm per day Sodium* iodide intravenously in doses of 1 gm per day may be substituted for the potassium iodide by mouth or may be used as a supplement.

In the usual pulmonary case there is adequate drainage through the bronchus but if such is not obtained or if the infection has extended into the *chest wall surgical drainage* is essential Since the sulfonamides protect against many of the secondary infections the surgeon can afford to be radical All sinus tracts should be explored and drained and the severely damaged tissues should be excised as

far as it is practical Lobectomy and pneumonectomy should be considered in selected cases which have failed to respond to other types of therapy

Penicillin in doses as small as 10 000 units every three hours or 80 000 units per day frequently results in rapid elimination of fever and marked clinical improvement in the patient The usual minimal dose at the present time is 1 million units daily Potassium iodide should be given as a supplementary treatment to increase the penetration of penicillin into the relative avascular areas of disease If progressive improvement does not begin in 7 to 10 days surgery should be considered Sulfonamides can be substituted for penicillin when the patient becomes ambulatory Sulfonamides and iodides should be continued for six months after the disappearance of symptoms to prevent relapses

NOCARDOSIS

Nocardosis like actinomycosis is world wide in distribution and pathogenic *Nocardia* have been isolated from the soil *Nocardia* are readily differentiated from *Actinomyces* by cultural reactions the former are aerobic and grow readily on simple laboratory media at room temperature while the latter are anaerobic and require a rich media at 37°C temperature Most pathogenic *Nocardia* are acid fast and may be confused with pathogenic tubercle bacilli atypical acid fast bacilli or even saprophytic acid fast organisms The characteristic branching of *Nocardia* should prevent this error

The tissue reactions are very similar to those seen in actinomycosis The same type of granulomatous lesions with focal abscesses are seen in both and typical sulfur granules may be induced by *Nocardia* Both show gram positive branching filaments in the tissues

The *clinical picture* as might be expected from the tissue reactions may be identical Primary involvement of the cervicofacial area and the abdominal organs is much less frequent in nocardosis while infections of the feet and lungs are more frequent (Fig 2) The pulmonary infections are somewhat more fulminating with the production of purulent sputum which may contain blood The organisms spread from the lungs to produce subcutaneous abscesses lesions in the abdominal organs and brain A metastatic abcess of the brain may arise from a small or even clinically inapparent lesion of the lungs This series of complications occur with both actinomycosis and nocardosis but is more characteristic of the latter

The *treatment* of nocardosis is quite different from that of actinomycosis Penicillin is not effective even in daily doses of 20 million units In contrast sulfadiazine and other sulfonamides seem to be specific This treatment was introduced empirically in 1944 by Benbow Smith and Grimson and has been confirmed by later clinical observations and by experiment in animals Four to six grams of sulfadiazine should be given daily to obtain a blood level of 8 to 10 mgs per cent It



Fig 2 Nocardosis showing involvement of the right lung The etiologic agent was the acid fast *Nocardia asteroides* Cured with sulfadiazine and potassium iodide (After Benbow Smith and Grimson *Am Rev Tuberc* 49 395 1944)

severely ill patients the dose may have to be increased to 8 to 12 grams to obtain a blood level of 15 to 20 mgs per cent Streptomycin is less effective than sulfadiazine but may be used as a supplementary treatment in doses of 1 to 2 grams daily The broad spectrum antibiotics in general are palliative rather than curative but they may be necessary to combat secondary infections Surgery and iodides are less often required in nocardiosis than in actinomycosis but should be used when indicated

ACTINOBACILLOSIS

Actinobacillus lignieresi caused "lumpy jaw" in cattle Cases of septicemia suppurative bronchopneumonia and endocarditis have been found in man The literature was reviewed by Curtis Halley and Bacon in 1944 Potassium iodide is a specific for the disease

STAPHYLOCOCCIC ACTINOPHYTOSIS (BOTRYOMYCOSIS)

Occasionally staphylococci produce chronic granulomatous lesions with definite granule formation which under the low power of the microscope resembles typical "sulfur granules" The clinical course of the disease resembles actinomycosis The organism grows readily as an ordinary *Staphylococcus* The treatment is surgical drainage supplemented by penicillin and potassium iodide

NORTH AMERICAN BLASTOMYCOSIS

North American blastomycosis is characterized by the formation of granulomatous lesions in various parts of the body but here is a marked predilection of the skin lungs and bones Blastomycosis is a relatively common mycotic disease We have seen nearly 100 cases in the past 20 years and Schwartz and Goldman ascertained with a questionnaire that there were 101 diagnosed and/or treated in the United States during the first 6 months of 1953 Except for an occasional case in Canada and England the infection has been found only in the United States

The disease is not spread from man to man but evidently is derived from some source in nature Newberne Neal and Heath collected from the literature 30 cases of spontaneous blastomycosis in dogs In one instance the serum from the dog fixed complement with antigens prepared from human strains Blastomycosis may occur in patients as young as five months or as old as 82 years but in the series of 347 cases collected by Martin and Smith more than 50 per cent were between the ages of 20 and 40 The disease occurs nine times as frequently in males as in females and all races seem to be equally susceptible

The infection may begin primarily in the skin and remain localized for months or years before it spreads to the internal organs Schwartz and Baum after a review of 60 cases proposed the revolutionary concept that practically all cases of blastomycosis are pulmonary in origin including most cases hitherto regarded as primarily cutaneous It is true that typical cutaneous lesions do follow pulmonary infections and when fully developed cannot be differentiated from primary cutaneous infections However a careful history will reveal that the infection began as a subcutaneous lesion and spread upward into the skin These secondary skin lesions are metastatic in origin and are scattered haphazardly over the body while the true primary cutaneous lesions begin on the exposed surfaces of the hands feet and face They spread to the other parts of the body where it is easy to scratch with a contaminated finger Many of the primary cutaneous lesions follow a minor but known injury to the skin The

primary reaction is definitely cutaneous not subcutaneous and this observation applies to satellite lesions produced by scratching It seems illogical to endow the organisms with the ability to produce a typical cutaneous lesion when it reaches the subcutaneous tissue through the circulation and deny its ability to infect the skin by direct inoculation The *chronic nature and relatively benign course* of primary cutaneous blastomycosis is analogous to primary cutaneous tuberculosis

Most cases of systemic blastomycosis begin with pulmonary infection In the fatal cases studied at necropsy 95 per cent had pulmonary infections and in more than half of the cases the most extensive lesions were found in the lungs The bones were found to be infected in 60 per cent with the vertebrae and ribs being involved most frequently The liver spleen and kidneys were invaded in about 40 per cent the nervous system in about 30 per cent and the prostate in about 20 per cent The lesions in the liver and spleen are usually quite small and these organs are not enlarged The intestinal tract is spared in most instances

The *onset* of pulmonary blastomycosis frequently is insidious The symptoms may resemble those of an ordinary subacute respiratory infection with dry cough some pain in the chest slight fever and mild dyspnea After a period of weeks or months the sputum becomes purulent and may contain blood As the pulmonary infection progresses the *dyspnea becomes more marked the fever is* higher there is a marked loss of weight and strength and the patient develops night sweats The pleura may be involved and sinuses may appear in the chest wall but this complication is much rarer in blastomycosis than in actino*mycosis*. The mediastinum frequently is invaded in the latter stages of the disease and Baker and Brian have shown that the pericardium and heart may be involved In the terminal cases with widespread dissemination symptoms referable to other internal *organs* may appear such as pain in the bones or prostate or paralysis from invasion of the *brain* and spinal cord

The *physical signs* of pulmonary blastomycosis are similar to those of pulmonary abscess or massive tuberculosis Percussion usually reveals dullness but rales are inconstant and variable *in type and distribution*

The *chest films* may show in early cases an enlargement of the mediastinal lymph nodes *without obvious parenchymal* lesions but lymph node involvement is relatively rare in blastomycosis in contrast to the findings in histoplasmosis coccidioidomycosis and sporotrichosis In most instances however dense masses are seen Such masses may be located near the hilum and project into the lung fields with irregular outlines This type of infection frequently suggests the diagnosis of neoplasm (Fig 3) especially when the pa



Fig 3 North American blastomycosis showing hilar involvement and tumor like *masses projecting* out into the lung fields The patient was [illegible]

completely and the one on the left was reduced to a small linear scar The patient was well *10* years later (*After Martin and Smith Am Rev Tuberc* 39 488 1939)

tient also has localized pain in the chest and blood in the sputum *There are many* reports in the literature where lobes or one entire lung have been removed for a supposed carcinoma of the bronchus only to discover by microscopic examination that the patient had *blastomycosis* This was an academic *not a therapeutic error before the discovery*

of a specific drug therapy for blastomycosis At present every effort should be made to eliminate the possibility of blastomycosis before sacrificing potentially good pulmonary tissue

Cavities are not characteristic and when present are usually small and have irregular hazy outlines Older patients particularly those with preexisting emphysema do develop 3 to 4 cm thin walled cavities In some instances the cavities persist for months and possibly years and the sputum is periodically or constantly positive for *Blastomyces* These *thin-walled cavities are difficult to differentiate from the thin* walled cavities which are such a characteristic residuum of primary coccidioidomycosis

Sometimes infection spreads through the body by way of the blood stream The pulmonary shadows may then resemble miliary tuberculosis except that they are a little coarser and are not quite as well defined When disseminated blastomycosis is suspected x rays should be made of the entire skeleton As in tuberculosis the bodies of the vertebrae may *be destroyed resulting in collapse with compression of the spinal cord The lesions* usually are less cyst like than those seen in coccidioidomycosis and are more destructive and less proliferative than those of actinomycosis In many instances however a differential diagnosis between these three diseases cannot be made from the films alone

As the disease progresses a hypochromic anemia develops there is an increase in the *sedimentation rate and an increase in the white blood count with a rise in the polymorphonuclear leukocytes*

A positive skin test to *Blastomyces* vaccine develops in the more extensive skin cases and in almost all of the systemic cases The dying patient however may be anergic Dr Donald S Martin in our clinic employs the complement fixation technique using as the antigen either the whole bodies of the organisms or a powdered extract The test frequently *is positive in the progressive cases but patients who recover eventually lose their antibodies and the* tests become negative

There is some cross reaction both in the skin test and in the complement fixation test in cases of blastomycosis and histoplasmosis *Histoplasma capsulatum* is the better antigen and larger skin tests are produced and higher complement fixation tests are obtained We use a 1 100 dilution of standard blastomycin histoplasmin and coccidioidin and give the three tests simultaneously If excessive sensitivity is suspected a 1 1000 dilution should be used Patients negative to the 1 100 dilution can be retested with a 1 10 dilution A negative reaction to this strong dose can be *accepted but a positive may be nonspecific The blastomycin reaction is usually maximum in 24 hours the coccidioidin in 48 hours and* the histoplasmin in 72 hours Patients with strong histoplasmin reactions usually give a smaller (approximately 20 %) reaction to blastomycin The converse type of cross reaction has been seen but it is relatively unusual The same type of cross reaction is seen in the complement fixation The serum of a patient with histoplasmosis having a titer of 1 200 for histoplasmin may have a titer of *1 80 with the Blastomyces antigen* In proven cases of blastomycosis *the titer may be only 1 20 or 1 40 with no crossing or crossing with only a 1 10 with histoplasmin In rare* instances the complement fixation titer may be higher to the cross reacting antigen This might be expected on the law of chance since the endemic areas of histoplasmosis and blastomycosis overlap and a patient with a previous subclinical infection with the one fungus might give a higher cross reaction than to the specific fungus at the beginning of an infection This anomalous situation may reverse itself *as the disease progresses*

The blastomycin skin test is not as reliable as the corresponding histoplasmin and coccidioidin At least 25 per cent of the early cutaneous and some of the early pulmonary cases have negative blastomycin tests when first seen although most of these developed positive skin tests as the disease progressed Subclinical infections with *Blastomyces dermatitidis* do occur We have seen 3 healthy *medical students and 10 patients with other diseases who had positive skin tests to a Blastomyces* vaccine skin test *and negative re*action to the histoplasmin In the epidemic of blastomycosis which occurred in Grafton

body and judged by clinical results it requires 15 to 20 days to accumulate a therapeutic level in the tissues and the therapeutic level after 30 days treatment persists for at least 6 months and possibly for a year or more We have treated approximately 18 cases with stilbamidine and 15 with 2 hydroxystilbamidine All were relatively early cases with symptoms from 1 to 6 months Only 3 patients have had relapses 2 after 6 months and one after 2 years All three relapsing cases have had bone lesions Two patients recovered after retreatment and surgical drainage the third had multiple lesions of the vertebrae and ribs which could not be drained and he has continued to relapse Kuhn has reported a case of cutaneous blastomycosis which failed to heal after several courses of stilbamidine and 2 hydroxystilbamidine and who was found to be hypersensitive to *Blastomyces* vaccine Desensitization with this vaccine was followed by healing without additional chemotherapy Theoretically the fungus might become resistant to the drug and subsequently relapse but this has not been demonstrated

The relapsing patients by history have usually been ill for many months and have had multiple organ involvement They have also received large amounts of the drugs It is possible but not proven that overdosing may lower the natural resistance of the patients tissues Certainly it is advisable to effect a cure with the smallest possible amount of the drug After our initial course of 30 days therapy we watch the patient for improvement We have regularly observed much more improvement during the first 30 days after therapy was stopped than we saw during the original treated period of 30 days The improvement then continued at a slow rate for 4 to 8 months If a relapse occurs every effort should be made to excise or drain the focus of infection midway in the new period of treatment

There are oral reports but no publication to the effect that patients who have had relapses after repeated courses of stilbamidine and/or 2 hydroxystilbamidine will respond to treatment with a new antibiotic called Amphotericin B

There is an oral form of 2 hydroxystilbamidine available for clinical investigation but its effectiveness has not yet been established

SOUTH AMERICAN BLASTOMYCOSIS

This mycosis may begin in the skin or mucous membranes but eventually involves the *lymph nodes* and internal organs including the lungs It is usually referred to in the literature as paracoccidioidal granuloma or Lutz Splendore-De Almeida s disease The name "paracoccidioidal granuloma was applied because the fungus in the tissues has a superficial resemblance to *Coccidioides immitis* the cause of coccidioidomycosis Recent cultural studies by Conant have shown that the fungus reproduces by the formation of multiple buds and for that reason it has been placed in the genus *Blastomyces* as *Blastomyces brasiliensis*

Most cases of this infection have been reported from Brazil although isolated cases are found in Argentina Paraguay Venezuela and Peru At the present time we have not found any reported cases which originated outside of South America

The *source* of the infection is not known but it occurs most frequently in manual laborers whose work brings their skin in contact with *vegetable material* Many of the cases have been found in workers on coffee plantations

De Almeida reviewed and analyzed 570 cases All races are susceptible males are infected 9 5 times as frequently as females and the highest incidence occurs between the ages of 20 and 30

De Almeida and other South American workers have described *four clinical types* of the disease *first* a cutaneous or mucocutaneous form which begins in the skin or mucosa most often in the region of the mouth and nose *second* a lymphatic type which begins as a localized lymph node enlargement most often in the neck but sometimes in the supraclavicular or axillary regions *third* a visceral form with involvement of liver spleen pan

creas and lungs and *fourth* a mixed type which involves both skin and internal organs

Many of the skin and mucosal lesions resemble cutaneous leishmaniasis Some simulate the dermal lesions of North American blastomycosis The lymph nodes are involved much more frequently in South American blastomycosis than in North American blastomycosis

In contrast to North American blastomycosis where pulmonary lesions are usually present involvement of the lungs in the South American disease is relatively late and not a striking part of the clinical picture The lungs are reported as being involved in 20 per cent



Fig 4 South American blastomycosis showing extensive patchy infiltration throughout both lungs There are some thin walled cavities at the right base and definite enlargement of the hilar lymph nodes (Courtesy of Dr F de Almeida Sao Paulo Brazil)

of the patients with the visceral type of infection The patient may have cough and purulent sputum which occasionally is blood streaked Rales may be present throughout the lungs but the lesions are rarely extensive enough to cause dullness to percussion

The diffuse nodular appearance of the pulmonary lesions as seen in x ray (Fig 4) and in postmortem studies suggests that the fungus invades the lungs secondarily by the hematogenous route Small thin walled cavities may be present but extensive cavity formation is rare

The *diagnosis* can be suspected from the appearance of the dermal and mucosal lesions but must be confirmed by biopsy and culture *Blastomyces brasiliensis* grows on blood agar at incubator temperature and on Sabouraud's medium at room temperature producing colonies which resemble very closely those of *Blastomyces dermatitidis* The mycologic diagnosis is established by demonstrating multiple buds on the yeast like organisms found on the blood agar cultures

Friedman and Conant found that patients and experimentally infected animals had complement fixing antibodies in the serum And as might be expected there were some cross reactions with North American blastomycosis and histoplasmosis They also found that patients with the North American disease gave positive skin reactions with antigens prepared from *Blastomyces brasiliensis* Conversely Lacaz and also Versiani report that patients with the South American disease give positive skin tests with blastomycin but not coccidioidin

The cutaneous and mucocutaneous lesions of South American blastomycosis must be differentiated from those of cutaneous leishmaniasis yaws syphilis tuberculosis and certain neoplasms The lymphatic and visceral types may be confused with visceral leishmaniasis tuberculous adenitis and peritonitis syphilis neoplasms aleukemic leukemia and Hodgkin's disease Other mycoses such as histoplasmosis coccidioidomycosis actinomycosis North American blastomycosis cryptococcosis and sporotrichosis must be eliminated

Before the introduction of sulfonamides the disease was invariably fatal De Almeida has reported some improvement in early cases with iodide therapy but he has observed that the iodides may accelerate the spread of the infection when the patient is already in an advanced stage of the disease The importance of desensitizing hypersensitive patients before the administration of iodides has already been discussed in connection with North American blastomycosis

At the present time Dr Domingos de Oliveira Ribeiro and others in Brazil are

treating this mycosis with sulfapyridine and sulfadiazine The patients are given 2–4 gms a day for many months There is a dramatic improvement in the general condition of the patient Unfortunately however many of these patients subsequently relapse and die of the disease It is possible that desensitization with a vaccine carried out concurrently with the sulfonamide might give better results or they might respond to stilbamidine 2 hydroxy stilbamidine or Amphotericin B

GEOTRICHOSIS

Geotrichosis is caused by one or more species of the genus *Geotrichum* The fungus produces lesions in the mouth intestinal tract, bronchi and lungs This mycosis is not very common and frequently produces relatively mild infections Certain forms of *Geotrichum* may be confused with *Blastomyces dermatitidis* which causes the highly fatal North American blastomycosis

It is probable that this infection is endogenous in origin since the fungus frequently is found in the mouths and intestinal tracts of normal individuals In a series of 314 stool specimens obtained from medical students nurses and patients without intestinal symptoms Schnoor cultured *Geotrichum* in 29 per cent

Bronchial geotrichosis is the most frequently recognized form of the infection The patient has symptoms which are identical with those of the ordinary chronic type of bacterial bronchitis. The sputum frequently has a peculiar mucoid or gelatinous consistency but only occasionally is blood streaked There is little if any evaluation of the temperature or pulse and the general health of the patient is not affected seriously although he is handicapped by the harrassing cough Physical examination shows numerous medium and coarse rales especially at the bases Chest films show a diffuse peribronchial thickening which is accompanied sometimes by fine mottling at the bases of the lungs or in the mid lung fields

Pulmonary geotrichosis simulates tuberculosis with an elevation of temperature pulse and respiration and leukocytosis The sputum is generally light in color and mucopurulent in contrast to the greenish purulent sputum of tuberculosis Frank hemoptyses may occur The organisms are present in abundance in the purulent or blood sputum and can be cultured without difficulty on Sabouraud's medium On physical examination there is usually dullness and altered breath sounds with fine and medium rales resembling those found in acute reinfection tuberculosis The x rays show smooth dense patches of infiltration which may or may not contain thin walled cavities The lesions may occur in any part of the lungs but are sometimes confined to the upper lobes (Fig 5)

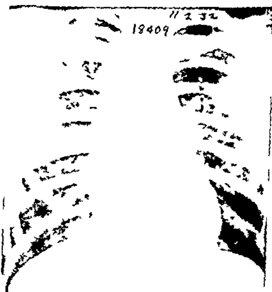


Fig 5 Geotrichosis of the lungs showing two small cavities in the right upper lobe and a larger one in the left upper lobe The lesions disappeared with potassium iodide therapy (After Smith J Thoracic Surg 3 241 1934)

The disease may be suspected from the presence of the peculiar mucoid gelatinous sputum but the diagnosis cannot be established without the demonstration of the organism both by direct examination and by culture Direct examination is essential because occasional colonies of *Geotrichum* may be found in cultures of oral secretions

from normal individuals After some of the sputum is treated with a drop of 10 per cent potassium hydroxide and examined directly under the microscope the fungus will be found as oblong or rectangular cells 4 by 8 μ with somewhat rounded ends or as large spherical cells 4 to 10 μ in diameter *Geotrichum* grows readily on Sabouraud's glucose agar at 37 degrees or at room temperature The appearance of the growth is quite different depending upon the temperature of incubation At room temperature most of the growth is down into the medium and the long hyphae develop septal walls and then break up into rectangular arthrospores These rectangular cells usually germinate by a germ tube from one corner which is a characteristic method of growth for cultures of *Geotrichum* At 37 degrees C the colony is smaller and grows more on the surface of the medium Short mycelia are produced with many more spherical cells 4 to 12 μ in diameter Some of these spherical cells have rather thick walls and may be confused with the budding form of *Blastomyces dermatitidis* but the presence of rectangular arthrospores establishes the diagnosis of geotrichosis

Geotrichosis must be differentiated from tuberculosis bacterial infection of the lungs and certain other mycoses particularly moniliasis North American blastomycosis cryptococcosis and coccidioidomycosis *Geotrichum* is not infrequently found in the sputum in association with Friedlander's bacillus and it is often impossible to determine which organism is the primary invader We have studied one patient with a chronic non tuberculous infection of the lungs of 20 years duration who has had in her sputum for over five years both Friedlander's bacillus and a species of *Geotrichum* *Geotrichum* may be a secondary invader in pulmonary tuberculosis In one patient with a mottled disease of the right upper lobe *Geotrichum* was present in abundance in the sputum by direct examination and culture and no tubercle bacilli could be demonstrated even by guinea pig inoculation Treatment with potassium iodide eliminated the cough and expectoration but six months later her symptoms returned and tubercle bacilli without *Geotrichum* were found in her sputum

The *prognosis* usually is good with geotrichosis One of the chief reasons for recognizing this infection as a specific entity is to avoid confusing geotrichosis with North American blastomycosis in which the prognosis is poor

The bronchial form of the disease responds readily to *treatment* with potassium iodide given by the rapid method described in the section on North American blastomycosis The pulmonary form of the disease should be treated by the same regimen employed in tuberculosis including rest in bed and a high vitamin diet A thorough study of the sputum for the presence of tubercle bacilli including guinea pig inoculation should be made before iodides are administered An autogenous vaccine should be tried if the patient does not respond to treatment with iodides

COCCIDIOIDOMYCOSIS

Coccidioidomycosis caused by *Coccidioides immitis* produces two different clinical types of infection Cases of primary coccidioidomycosis occur by the tens of thousands in the arid regions of the southwestern part of the United States The infection is an acute but benign self limiting respiratory disease Approximately 1 per cent of the primary cases develop into progressive coccidioidomycosis which is a chronic malignant disseminated disease involving the cutaneous subcutaneous visceral and osseous tissues

Emmons discovered that coccidioidomycosis is an endemic disease of rodents in the arid regions of the Southwest The organism has been isolated repeatedly from the soil and may be introduced into the skin following an injury but more often it is breathed into the lungs of men and animals with dust particles Naturally occurring infections have been found in cattle sheep and dogs but there is no evidence that man acquires the disease directly from either human or animal sources

The *symptoms* of primary pulmonary coccid

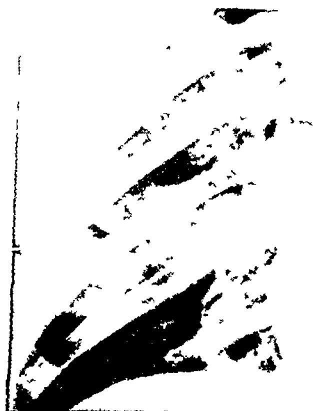


Fig 6 Primary coccidioidomycosis showing soft nodular lesions which were found 13 days after a known exposure to dust containing arthrospores of *Coccidioides immitis* and 4 days after the sudden onset of symptoms (After Powers and Starks *Radiology* 37 445 1941)

ioidomycosis resemble those of a mild upper respiratory infection although occasionally they are much more severe and simulate a lobar or lobular pneumonia (Fig 6) An epidemic which occurred in a group of 75 soldiers was reported in detail by Goldstein and McDonald The incubation period varied from one to three weeks Fever was present in 100 per cent cough 88 per cent pain in the chest 88 per cent chills 66 per cent sputum 65 per cent sore throat 37 per cent and hemoptysis 18 per cent of these patients *Physical signs* were present in only 26 per cent and these were largely limited to alterations in breath sounds Dullness to percussion and rales were rare In this series erythema nodosum developed in 19 per cent erythema multiforme in 2 6 per cent morbilliform rash over the trunk and lower extremities in 4 per cent and arthralgia in 28 per cent These allergic reactions appeared in 8 to 14 days after the onset of symptoms and usually were accompanied by eosinophilia In a few instances the initial symptoms were those of pleurisy with effusion but more often the dry type of pleurisy developed with severe pain in the chest

Colburn made x ray studies of the 75 soldiers with primary pulmonary coccidioidomycosis reported by Goldstein and McDonald Although severe clinical symptoms were present there were no detectable x ray changes in 4 per cent of this group Fan shaped densities extending out from enlarged hilar nodes were present in 38 7 per cent These shadows required an average time of 40 days for resolution although the extremes were 15 and 90 days respectively In 24 per cent hilar lymph nodes were present without detectable parenchymatous lesions In an additional 26 per cent there were both peripheral and sublobular infiltration which occurred in the upper and lower lobes Thin walled pulmonary cavities which are characteristic of the disease developed in only 4 per cent Some of these cavities healed in 60 days and some in 95 days while others persisted Cavities of this kind have been known to persist for years

Occasionally calcification occurs both in the periphery of the lungs and in the hilar lymph

nodes These calcifications are difficult if not impossible to differentiate from calcifications which follow a primary infection with the tubercle bacillus Cox and Smith have shown that *C immitis* can be recovered from calcified foci many years after the initial infection

Occasionally spherules containing the typical endospores can be found by direct examination of the sputum The organisms grow readily in the mold like form when cultured on Sabouraud's medium although they may not have been demonstrated by direct examination of the fresh sputum A *positive skin test* to coccidioidin appears during the first week of symptoms and reaches 99 per cent by the end of the third week The standard dose is 0 1 cc of a 1 1000 dilution of a standardized coccidioidin If extreme sensitivity is suspected the initial dose should be 0 1 cc of a 1 10 000 dilution

Patients who fail to react to the 1 1000 test of coccidioidin should be retested with a 1 100 and finally with a 1 10 dilution The test is performed like a tuberculin test and read after 24 48 and 72 hours Patients with strong skin reactions show smaller cross reactions with histoplasmin and occasionally small cross reactions with blastomycin

About 50 per cent of patients with primary infections have a *positive precipitin test* by the end of the first week of symptoms and 90 per cent are positive by the end of the third week However an occasional patient does not develop precipitins until the 6th week Usually the precipitins begin to fall in titer after the 3rd week reaching a low of 10 per cent after 6 months The *complement fixing antibodies* develop more slowly only 10 per cent of patients are positive at the end of the first week of symptoms and only 65 per cent after 2 months Mild clinical subclinical and small localized infections usually do not stimulate the tissues sufficiently to induce a detectable level of complement fixing antibodies The more extensive and severe the infection the higher is the complement fixing titer In the terminal stages of the disease the skin test may be negative but the complement fixing titers continue to increase Patients with a high level of antibodies in the serum do not have antibodies in the spinal fluid unless there is a concurrent infection of the brain Not all patients with cerebral involvement have antibodies in the spinal fluid but in some instances the spinal fluid is positive when the serum is negative In all forms of the disease the decline in the complement fixing antibodies follows clinical improvement and negative tests are obtained some months after the infection has been eliminated

Reciprocal relationship between the precipitin and complement fixation titer is of major importance in *prognosis* *A progressive decrease in the precipitin titer accompanied by a rapid increase in the complement fixation titer indicates that the patient is developing the highly fatal progressive form of coccidioidomycosis*

Practically all of our exact knowledge about skin tests and serology in coccidioidomycosis has been worked out by Dr C E Smith and his associates in California during the past 20 years Access to the details of these studies can be obtained through the references given in the bibliography

Among the soldiers studied in the Southwest only about 0 2 per cent of the cases of primary infection in the Caucasian race proceeded to the development of the progressive and usually fatal form of the disease It has been estimated that Negroes Mexicans and Filipinos are about 20 times as likely to develop the progressive form of the disease as are representatives of the Caucasian race

In many instances the primary form of the disease develops directly into the progressive form If fever persists and new lesions appear in the parenchyma of the lungs or if subcutaneous or bone lesions occur the diagnosis of the progressive form of the disease is obvious In other cases the patient makes a partial but not complete clinical recovery and an interval of some months may elapse before the onset of the progressive type of infection Some instances of progressive coccidioidomycosis terminate fatally within a few months but in other cases the patient may live for a year or more These patients have a continuous low grade fever marked anorexia and rapid loss of weight and strength Dyspnea and cyanosis may be extreme as the

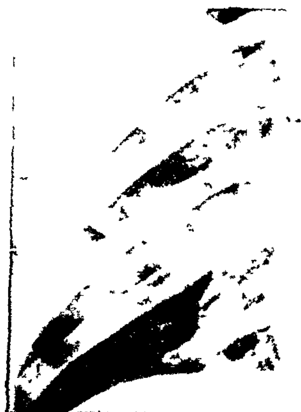


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pulmonary infiltration increases The sputum is mucopurulent and sometimes bloody and usually *contains many of the characteristic* fungus spherules Invasion of the bones joints skin subcutaneous tissues internal organs brain and meninges occurs with great regularity Occasionally coccidioidal meningitis *is found in patients who show no evidence* of the primary portal of entry

The progressive form of the disease should be suspected if the shadows found in the primary form persist for more than six weeks *The diagnosis of the* progressive form is almost certain if new lesions appear in the chest or if tuberculous like infiltrations develop in the apical or subapical areas A progressive increase in mediastinal adenopathy is a bad sign When progressive coccidioidomycosis is suspected the entire skeleton should be x rayed The typical lesion in the bones appears as a sharply circumscribed area of destruction with little or no reaction in *the surrounding bones Such lesions* are cyst like in appearance and vary from 0 5 to 3 cm in diameter Although any bone in the body may be involved the ribs vertebral bodies small bones of the hands and feet tibial tubercles *malleoli olecranon styloid processes* acromial processes and the angles of the scapulae are most often invaded in the order named A terminal miliary dissemination to the lungs is not unusual

Sputum and *exudates* should be examined directly in 10 per cent sodium hydroxide for the presence of the typical spherules which are thick walled structures 20 to 80 μ in diameter containing numerous small endospores 2 to 5 μ in diameter Sputum and other materials should be planted on Sabouraud s glucose agar and incubated at room temperature On this medium the organism develops after ten days or two weeks a moist, membranous colony which remains closely applied to the surface of the agar With further incubation an abundant cottony aerial mycelium *appears which is white at first* but becomes tan to brown with age The typical microscopic picture shows the presence of numerous thick walled rectangular ellipsoidal or spherical arthrospores about 2 5 to 3 by 3 *to* 4 μ *in size* These arthrospores are highly infectious a number of laboratory infections have resulted from their inhalation

Coccidioidomycosis should be suspected in every obscure illness originating in a person living in an endemic area or in individuals who have visited such areas at any time Primary coccidioidomycosis may be diagnosed incorrectly as common cold bronchitis influenza bronchial pneumonia or primary atypical pneumonia of unknown etiology Progressive coccidioidomycosis must be differentiated from tuberculosis syphilis glanders tularemia bacterial osteomyelitis neoplasms and other mycoses particularly blastomycosis actinomycosis cryptococcosis sporotrichosis and mycetoma

The *prognosis* is excellent in primary pulmonary coccidioidomycosis and it is good in the cutaneous and glandular types of primary infection In progressive coccidioidomycosis the prognosis is very grave The mortality is usually given as 55 to 60 per cent but it is probably *much higher than this since the primary* benign type of the disease was not differentiated from the more severe progressive form of the disease in the earlier reports in the literature

The *treatment* for primary coccidioidomycosis is symptomatic The patients should be kept in bed until their temperature white blood count and sedimentation rate are normal and their x ray films are either normal or showing progressive clearing The small residual cavities usually heal in less than one year (Fig 7) The larger cavities particularly when complicated by repeated hemoptyses may require lobectomy

The antibiotics are useless for therapy and cortisone and other corticosteroids may increase the speed of dissemination We have *seen rapid clinical improvement in one patient* following the use of 2 hydroxystilbamidine when the drug was given daily for 30 days This case was in a physician with a laboratory acquired infection and the treatment was started before the end of the second week of illness Some improvement even in cases of coccidioidal meningitis have been observed by others Somewhat more encouraging results have been reported for aminostilbamidine by Kushner Snapper and McMillen It may

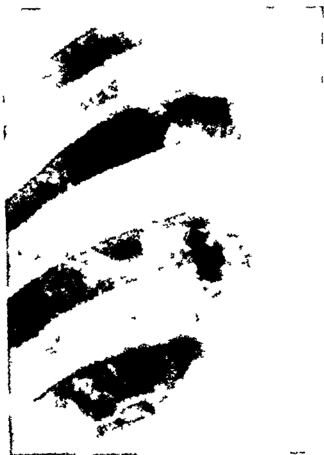


Fig 7 Primary coccidioidomycosis showing the thin delicate wall of the cavity The cavity began to close by the twenty ninth day of the disease After 1 year there was a cyst like shadow in the region and one single small nodule in the periphery of the lung the hilar nodes were much denser suggesting the possibility of calcification The patient was clinically well (After Powers and Starks *Radiology* 37 448 1941)

be predicted that neither of these diamidines will become the definitive therapy for this disease since both are essentially fungistatic rather than fungicidal Amphotericin B has been used in a few cases with rather dramatic improvement This antibiotic certainly deserves a thorough trial

CRYPTOCOCCOSIS

Cryptococcosis caused by *Cryptococcus neoformans (Torula histolytica)* may involve the skin and other parts of the body but has a marked predilection for the lungs and for the brain and meninges The mycosis caused by this fungus generally is referred to in the European literature as blastomycosis or Busse Buschke's disease In the American literature we find the term "European blastomycosis" which is used to distinguish cryptococcosis from North American blastomycosis or Gilchrist's disease In the older American literature most instances of the disease will be found indexed as torulosis

Cryptococcus neoformans has been found in all parts of the world It has been reported in children less than 10 years of age and in adults of more than 70 but most of the cases have occurred between the ages of 40 and 60 All races seem to be equally susceptible and almost as many females are infected as males

The organism has been isolated from normal human skin by Benham and from a variety of sources in nature including the soil milk

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sional report describing the presence of agglutinating and complement fixing antibodies in the sera of the infected patients most observers have failed to demonstrate any serologic evidence of infection The large mucoid capsule which is characteristic of the appearance of the organism in tissue may inhibit antibody production Benham was unable to produce agglutinins or precipitins in rabbits by injection of the whole yeast cells Antibodies were formed however if the animals were injected with cells from which the capsular material had been removed by chemical methods

We have never succeeded in demonstrating agglutinins in the serum or spinal fluid of patients with cryptococcus meningitis These patients also fail to give positive skin reactions to vaccines prepared from their own organisms Under favorable conditions spontaneous cures of localized pulmonary infections probably occur with some frequency but are not detected We have seen two pulmonary infections in which the patients had a good high titer of agglutinins in their serum and one of these had a positive skin test to an autogenous vaccine Since Evans and Kessel have shown that there are at least three different immunologic capsular types of *Cryptococcus* the patients own culture should be used for agglutination test and for skin tests

There is nothing characteristic about the pulmonary symptoms signs or x ray pictures of patients with cryptococcosis The diagnosis of primary pulmonary cryptococcosis usually is made by routine cultures of the sputum on Sabouraud s medium and this should always be done in every case of obscure pulmonary infection The organism grows as a soft creamy white mucoid colony When some of the culture is mixed with India ink and examined under the microscope the large capsule can be seen surrounding budding yeast cell

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The prognosis is grave in all forms of cr coccosis Most of the primary pulmonar fections have spread eventually to the l and meninges and produced death How it is possible that some of the pulmonar fections may heal spontaneously without diagnosis every being established

The disease can be cured by surgic cision if the entire area of infection e pulmonary lobe is removed before the n tion has spread to the brain

Although occasional patients have covered following treatment with sulfadi actidione aromatic diamidines and agents in general these drugs have been disappointing The most promising dru the moment, at least for temporary reco is *Amphotericin B* This new antibiotic, a new species of *Streptomyces* has a rem able affinity for the organisms It is s what toxic and must be administered venously over a six hour period each da 30 to 60 days The dose is graduall creased from 0 25 mg to 1 mg per kilo of body weight as the patients demons their ability to tolerate the drug One pa with Cryptococcus meningitis treated in hospital with Amphotericin B now has n tive cultures and negative protein and cyto and appears to be well clinically We heard of a number of similar cases with s lar dramatic short time recovery If t patients remain well this may indeed be specific therapy which has been sough vain over the past 40 years

MONILIASIS

A number of species of *Monilia* or *Candida* may be found as normal inhabitants of the mouth and skin Only *Candida albicans* (*Monilia albicans*) is potentially pathogenic and even this species may be present as a saprophyte without producing any reac in the host *C albicans* may produce les in the mouth vagina, skin nails bronch lungs and occasionally a septicemia en carditis or meningitis Both local and gen

and fermenting fruit. Emmons isolated pathogenic strains from soil contaminated by milk and from a number of samples of pigeon manure. The patient whose x-ray is shown in Fig. 8 was exposed to pigeon and chicken manure prior to the development of pulmonary symptoms.

The *symptoms* of primary pulmonary infections are not diagnostic. The patient presents the picture of a subacute infection with low grade fever and mild cough. In some instances there *is no sputum*, *in others* a small amount of mucoid sputum is produced



Fig. 8. Chronic *cryptococcosis of the lungs of* some 3 years duration. Diagnosis established by *lobectomy*.

which rarely is blood stained. The lesions may develop in any part of the lungs and they are frequently bilateral but may be unilateral and confined to one upper lobe (Fig. 9). Dullness and altered breath sounds usually are found but rales are inconstant except in patients where there is a terminal miliary dissemination to the lungs. The patient may have a mild respiratory infection with minimal signs and symptoms and apparently be on the road to recovery when the infection spreads to the brain or meninges precipitating the cerebral type of the disease.

In primary pulmonary infections the shadows are often dense resembling a *massive* tuberculous lesion or neoplasm. Cavity formation is unusual and the *mediastinum rarely is* involved. *The patient whose film appears as* Fig. 8 *was originally diagnosed as a case of* chronic fibrocaseous tuberculosis or as chronic *organized pneumonia. The radiolucent areas* were thought to be multiple small cavities and *the denser areas fibrous tissue. The lobe* was removed by surgical excision. The apparent *cavities were emphysematous areas* surrounded by fibrous and granulomatous tissue. Numer-

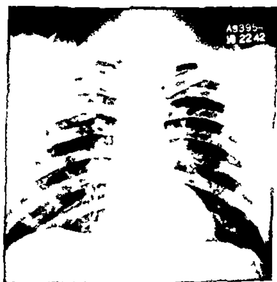


Fig. 9. Cryptococcosis of the lungs showing a round sharply circumscribed mass in the right upper lobe. The lesion subsequently extended *and simulated the picture of lobar* pneumonia. The patient died after an extension to the brain.

ous typical encapsulated *Cryptococcus neoformans* were found in the tissues and recovered by cultures. This is the first instance of chronic cryptococcosis of the lungs to be recognized in the Duke Clinic.

Miliary lesions may be present throughout the lungs following the terminal dissemination of the fungus. Bone lesions may occur but they are rare in cryptococcosis in contrast to the frequency with which they are found in actinomycosis, North American blastomycosis and coccidioidomycosis.

Although the literature contains an occa-

mon and effusions occur occasionally. The cough is harassing and the patient produces mucoid gelatinous sputum which sometimes is blood streaked. When secondary infections occur with pyogenic cocci the sputum is purulent. The areas of infection are of the lobular or bronchopneumonic type and are frequently scattered in two or more lobes. Occasionally an entire lobe is involved. Medium moist rales are present over the areas of involvement, but dullness and changes in the breath sounds are variable. In the most severe infections the physical signs are those of a confluent or lobar pneumonia with dullness, increased tactile fremitus, whispered voice and prolongation of expiration. The x ray shadows in pulmonary moniliasis vary in size and shape and resemble those seen in bronchopneumonia except that the edges of the lesions usually are less sharply defined (Fig 11). Two or more lobes frequently are involved although the apices of the lungs usually are spared. Some lobes may show almost complete consolidation while others contain bronchopneumonic patches. The lesions are very labile and films made at weekly intervals show definite evidence of clearing in some areas and spreading in others.

Agglutinins have been demonstrated in the sera of patients with moniliasis and sometimes the titers are as high as 1:2400. They are not constantly present and we have seen patients with severe infections who had no demonstrable agglutinins in the blood. A large percentage of apparently normal individuals gave positive skin reactions when injected intradermally with vaccines or extracts of *C. albicans*. These findings are not surprising in view of the fact that the fungus is so frequently present on the skin and in the mouths and feces of normal individuals. A positive or negative skin test has little diagnostic value but skin tests should be performed on all patients with positive cultures for *C. albicans* because the clinical course and management of the individual patient depend in part on whether or not the patient is hypersensitive to the fungus.

To establish the diagnosis of moniliasis one should find the budding yeast like organism by direct examination of sputum or exudates and isolate it in pure culture on Sabouraud's medium. It is necessary to establish the fact that the *Monilia* isolated is the potentially pathogenic *C. albicans*. If agglutinins are present in the patient's serum we are justified in concluding that the fungus has actually invaded the pulmonary tissues but agglutinins are not always present and even when present they may represent the response to a secondary Monilia invasion. *Every effort should be made to find a primary cause for the pulmonary lesion before accepting C. albicans as the etiologic agent.* In many instances a definite diagnosis cannot be established without the help of the therapeutic test. If the patient responds to specific treatment and the lesions disappear from the lungs then we are justified in concluding that *C. albicans* was probably the cause of the disease.

Bronchopulmonary moniliasis must be differentiated from ordinary bronchitis and the pulmonary form from common pyogenic infections as well as certain of the mycoses such as cryptococcosis, blastomycosis, actinomycosis and coccidioidomycosis.

The acute cases of bronchopulmonary moniliasis which do not heal spontaneously develop into the chronic recurring form of the disease which may persist for years. The more severe pulmonary form of the disease runs a shorter course. An occasional patient dies after two or three weeks but in most instances there is complete recovery after four to six weeks. Occasionally recovery is not complete and the original pulmonary form of the disease changes over to the more chronic bronchopulmonary form.

Bronchopulmonary moniliasis responds readily as a rule to *treatment* with potassium iodide. The iodide should be given by the rapid method described in the section on North American blastomycosis. Ethyl iodide inhalations were employed successfully by MacKee in treating an apparently hopeless case of systemic moniliasis. Before iodides are administered the patient should be given a skin test with a heat killed *C. albicans* vaccine to determine the degree of sensitivity to the fungus. *Hypersensitive patients should be desensitized before iodides are administered.* The dilutions and doses are calculated

ized infections seem to increase in patients treated for prolonged periods with either broad *spectrum antibiotics* or with cortisone and other corticosteroids A fatal type of moniliasis, characterized by a lymphocytosis, has been described in at least five patients

In each instance it must be determined whether the *C albicans* is the primary cause of the disease or a secondary invader in some preexisting infection Moniliasis occurs at all *ages, in all races and* in both sexes

Bronchopulmonary moniliasis is the term used to designate that type of Monilia infection of the lungs where the disease is confined to the bronchi with a minimum amount of involvement in the peribronchial tissues The term pulmonary moniliasis is reserved for infections involving the parenchyma of the lungs

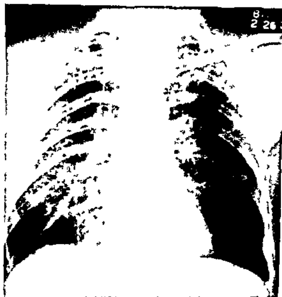


Fig 10 Bronchopulmonary moniliasis, showing diffuse linear shadows and small hazy nodules scattered throughout both lung fields The patient made a complete recovery following desensitization with an autogenous Monilia vaccine, followed by potassium iodide therapy

Bronchopulmonary moniliasis is not an uncommon infection A cough is the most characteristic and distressing *symptom* The sputum is almost colorless, but mucoid and *gelatinous, and frequently* contains small gray flakes composed of budding fungous cells and deteritus The temperature is normal or only slightly elevated, and the health of the patient is not affected seriously The infection sometimes disappears spontaneously but often lasts for years with periodic progressions and retrogressions The *physical signs* are those of bronchitis with medium and coarse rales at one or both of the lungs A particular type of *bronchopulmonary moniliasis occurs in the* tea tasters of Ceylon and has been described in detail by Castellani The *x-ray films* of patients with bronchopulmonary moniliasis usually show little more than a nonspecific type of peribronchial thickening Sometimes

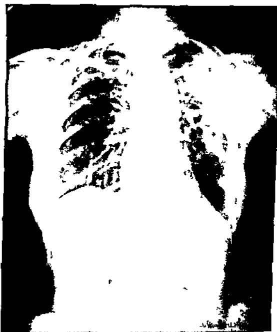


Fig 11 Moniliasis of the lungs, showing a homogenous pneumonic shadow in the left upper lobe The residue of a similar shadow can be seen in the right upper lobe The patient made a complete recovery after intravenous treatment with gentian violet

a peculiar hazy type of linear fibrosis can be seen (Fig 10) Although this picture is not diagnostic, Dr Robert J Reeves, of Duke Hospital, often suggests the possibility of moniliasis from the appearance of the film, and cultures very frequently have confirmed his tentative diagnosis

Pulmonary moniliasis is not as common as the bronchial form but is a more severe disease There is a moderate elevation of the temperature and pulse, pleural pain is com

defined cavity Large amounts of purulent sputum were produced which were negative for tubercle bacilli but contained filaments of *Sporotrichum* and the fungus was isolated on artificial media *Sporotrichum* also was isolated from samples of tobacco with which the patient had been working After treatment with potassium iodide there was rapid improvement in the clinical condition of the patient a marked reduction in the amount of sputum and the pulmonary shadows decreased to a small wedge shaped lesion which subsequently completely disappeared A metastatic lesion of the mastoid cells developed which required operation and more iodide therapy before the patient was entirely well

The third case was reported by Warfield in 1922 This patient had the disseminated subcutaneous lesions of sporotrichosis The chest films showed the right apex to be clear but the left apex was slightly hazy Extending out from the right hilum was a large somewhat circular shadow about 6 cm in diameter Radiating from the edge of this solid mass were fine linear markings extending into the first interspace and outward to the edge of the outer zone The left hilum was increased in size and there was some fine spotting along the left border of the heart The patient died although treated with arsphenamine and potassium iodide A *Sporotrichum* was isolated from the subcutaneous gummatous lesions during life and from various parts of the body at necropsy This strain produced nodular lesions in the lungs of albino rats even when the inoculation was subcutaneous Spores from the *Sporotrichum* were agglutinated by serum from this patient in a dilution of 1 150 Control sera gave no agglutination

The fourth case was reported by Nicaud in 1926 The patient had an encapsulated mass involving the lungs and pleura and *Sporotrichum* was grown from material secured by thoracentesis

The fifth case was reported in detail by Forbus in 1927 For three years the patient had dyspnea on exertion cough and a moderate amount of mucoid sputum which was occasionally blood streaked Fifteen months later the x ray films showed mediastinal shadows suggesting enlarged lymph glands No tubercle bacilli could be found in the sputum and the tuberculin was negative The symptoms gradually increased until she had stridor with inspiration and expiration wheezing and sibilant rales throughout both lungs By x ray the shadows had extended from the hilum into the lung fields on both sides Dr Charles L Minor of Asheville N C suggested the diagnosis of a tracheobronchial adenopathy of mycotic origin She was restudied at The Johns Hopkins where Minor s clinical findings were confirmed and a positive Wasserman discovered Dr W S Thayer of Baltimore followed the case with great interest He advised treatment with arsphenamine which was not effective and the patient died September 4 1917 The necropsy was performed by Dr Admont H Clark and *Sporotrichum* was grown in pure culture from the lungs by Dr Greenspon

In 1935 Moore and Kile reported a sixth case of generalized sporotrichosis with pulmonary involvement The x ray films showed enlargement of the hilar shadows and a fine nodular diffuse infiltration throughout both lung fields (Fig 12) A pure culture of *Sporotrichum* was isolated from an unopened subcutaneous nodule The organism could not be grown from the sputum After two months of iodide treatment there was a marked reduction in the parenchymatous pulmonary infiltration although the hilar shadows were still prominent The patient was reported as well four months after treatment was started

We have seen at Duke Hospital one instance where *Sporotrichum Schenckii* was associated with a pulmonary disease The patient was a child of 10 years and she presented the clinical picture of asthmatic bronchitis X ray films showed enlarged hilar lymph nodes resembling those seen in primary tuberculosis but she failed to react to an intradermal test with 1 mg (1 100) of old tuberculin *Sporotrichum Schenckii* was isolated from the sputum her blood serum in a dilution of 1 1000 agglutinated a suspension of Sporotrichum spores from her culture and an autogenous vaccine gave a positive skin test of the immediate type

By 1915 Meyer had collected 100 cases of

in the manner described in the section on North American blastomycosis

Intravenous gentian violet has been recommended by Stovall and others in the treatment of pulmonary moniliasis The dose of gentian violet is 5 mg per kilogram of body weight, and it may be repeated daily every day for three to seven doses Undesirable reactions can be avoided if commercially prepared solutions of gentian violet are used, but solutions made in the laboratory are safe if the concentration of the dye does not exceed 0.5 per cent and the solution is filtered through a Berkefeld or a Seitz filter Thrombosis of the veins may occur in patients who are injected with more concentrated solutions of the dye

The new antibiotic, Nystatin produced by *Streptomyces noursei*, seems to be remarkably effective in the treatment of oral, genital, gastro intestinal, and localized cutaneous forms of moniliasis The drug is not readily absorbed from the intestinal tract and therefore has a limited effect on pulmonary and systemic infections The still newer antibiotic *Amphotericin B*, should be tried in the apparently hopeless infections

SPOROTRICHOSIS

Sporotrichosis caused by *Sporotrichum Schenckii*, is a chronic infection with nodule formations in the lymph nodes, skin and subcutaneous tissues which soften and break down to form indolent ulcers

The disease may develop at any age from 16 months to 71 years but is most common between 20 and 40 About 10 per cent of the cases occur in children All races are susceptible, males are infected nine times as frequently as females and the disease is most prevalent in farmers, laborers and horticulturists

Sporotrichosis is world-wide in distribution The fungus grows as a saprophyte or as a parasite on certain plants, and spontaneous infections have been observed in horses, dogs cats, rabbits and rats Pathogenic sporotrichia have been found in the mouth and on the fur of healthy rats and Meyer recovered it from the coats of healthy horses Meyer infected himself with a culture isolated from a horse and Foerster reported two instances of the disease being acquired by handling contaminated dressings from a patient The study by Lurie and the one by Norden in our laboratories have shown that there is only one antigenic type of *Sporotrichum Schenckii*

Since the classical work of de Beurmann and Gougerot in 1912, the disease usually is described as conforming to one or more of the six different clinical types, namely, (1) lymphatic, (2) disseminated, (3) epidermal, (4) mucosal, (5) skeletal, and (6) visceral In this country the lymphatic is the predominant type of infection In the 109 cases collected by Foerster, the initial lesion was on one of the extremities in 90 instances

Apparently the disseminated form of the disease is seen more frequently in France than in the United States The epidermal, mucosal, skeletal and visceral forms are relatively rare Pyelonephritis, orchitis, epididymitis and mastitis have been reported

Pulmonary sporotrichosis is a relatively rare disease, and the critical review by Forbus of the reported cases shows that the evidence was inadequate to justify the diagnosis in most instances De Beurmann and Gougerot collected six cases from the literature, four they dismissed, but two were accepted as cases of pulmonary sporotrichosis Since 1912 Forbus has collected four other cases and reported one of his own In the first of the new cases, reported by Laurent in 1913 *Sporotrichum* was isolated from disseminated lesions, including infections of the bone, but the organism was not grown from the sputum The pulmonary signs were extensive, and all the lesions of bones, skin and lungs disappeared following treatment with potassium iodide

In the second case, reported by Dominquez of Havana Cuba, in 1914, there was some elevation of temperature accompanied by marked malaise, weakness and loss of weight The physical signs suggested tuberculosis or chronic pneumonia The chest film resembled an ordinary pulmonary abscess with a well-

solution X ray therapy is indicated as a supplementary treatment for particularly indolent lesions Vaccine therapy for desensitization may be tried if the response to iodides is unsatisfactory and if this fails a course of hydroxystilbamidine should be tried

HISTOPLASMOSIS

Histoplasmosis was not proved to be a mycosis until about 1934 The disease has been reported from South America North America Central America England South Africa the Philippines and Java All races seem to be equally susceptible The youngest patient was one month and the oldest 70 years but approximately 28 per cent of the cases were in children less than 13 years of age

The saprophytic form of *Histoplasma capsulatum* fungus has been isolated from soil by Emmons and by Furcolow and his associates The largest number of isolates have been from old deposits of pigeon chicken and bat manure or from soil fertilized by these materials The organisms survive and presumably multiply in enriched soil Loosh and his co workers isolated the fungus repeatedly over a period of years from the soil in an old silo Histoplasmosis has been reported in dogs cats house rat roof rat mouse skunk opposum fox cow horse and ferret, but there is no evidence that man is infected from these animals

The tissue form of the fungus grows in the cytoplasm of monocytes and in the endothelial cells of blood vessels and lymph nodes The organisms are quite small oval bodies 1 to 5 μ in diameter Often 50 to 100 such bodies are found in the cytoplasm of a single cell Smears of bone marrow splenic pulp lymph nodes sputum or even peripheral blood should be stained with a good blood stain such as those of Giemsa or Wright The tissue form of the organism can be grown on enriched media such as brain heart infection glucose blood agar When culturing contaminated material such as sputum or gastric washings 20 units of penicillin and 40 units of streptomycin should be added to each ml of media before pouring the petri dishes Small moist dull white colonies appear on the media without antibiotics after 7 to 14 days incubation at 37 C The colonies are rather atypical on the antibiotic containing media appearing as small membraneous cerebriform colonies which vary in color from pink to reddish brown These revert to typical colonies when subcultured on media without antibiotics

The saprophytic form of the organism grows on Sabouraud s glucose agar when incubated at room temperature After 15 to 20 days incubation a white cottony aerial mycelial growth appears On further incubation a buff to brown color appears and one can demonstrate the large 7 5 to 15 μ tuberculate spores which are diagnostic

There are a number of clinical types of histoplasmosis which are so diverse in their manifestation duration and prognosis that each must be discussed separately as distinct sub entities These are (1) *subclinical infections* (2) *localized primary pulmonary* (3) *diffuse primary pulmonary* (4) *localized mucosal or intestinal infections* (5) *disseminated primary infection* (6) *subacute primary infection* (7) *epidemic histoplasmosis* and (8) *reinfection histoplasmosis*

The vast majority of histoplasma infections are *subclinical* or at least produce symptoms which cannot be differentiated from mild intercurrent bacterial or viral infections Nevertheless the organisms induce a relatively permanent type of allergy which can be detected by a histoplasmin skin test Approximately 50 per cent of these individuals with positive skin tests will show by x ray from 10 to 200 small smooth oval calcified spots in the lungs and these are frequently accompanied by calcium deposits in the hilar lymph nodes (Fig 13) Lehan and Furcolow have estimated from the skin testing surveys made by Christie by Palmer by Furcolow and by Loosh that about 30 million individuals in the central portion of the United States have had primary subclinical infections with *Histoplasma capsulatum* In some areas 80 per cent of the population will react to histoplasmin

sporotrichosis from the literature, and several hundred more have been diagnosed since that time Even if one accepts all nine of the cases referred to above as authentic examples of pulmonary sporotrichosis, this is an astonishingly small number. Probably all cases of lymphatic sporotrichosis, and certainly all cases of the disseminated disease, should have the lungs studied by x-ray Since *Sporotrichum* has a predilection for lymph nodes in other parts of the body, enlargement of the tracheobronchial lymph nodes would be expected When sputum is present, even though scant in amount and mucoid, it should be streaked over a number of blood agar and Sabouraud's dextrose agar slants, one-half of which should be incubated at 37 degrees C and the others at room temperature The tubes should be examined every four days, but should be kept for four to six weeks The colonies which appear on these initial cultures, especially when bacteria are present, are much smaller than those of other mold-like fungi The colonies are small, circular in shape, *white in color and have a silk-like sheen* There are no aerial mycelia, but short root-like mycelia may penetrate the agar beneath the colony Recently Campbell has found that the tissues form of *S Schenckii* can be grown on the glucose cystine blood agar which Francis introduced for the cultivation of *Pasteurella tularense* It has not yet been determined whether this medium has any advantage over Sabouraud's glucose agar for the primary isolation of the organism

One cannot question the statement that sporotrichosis of the lungs is a rare disease, but probably it occurs much more often than a review of the literature would indicate Routine cultures for fungi should be made in all obscure pulmonary diseases and the cultures examined with care at periodic intervals, and from time to time the investigators will be rewarded with an unusual diagnosis—even a case of pulmonary sporotrichosis

Unfortunately, the growth of a *Sporotrichum from the sputum* will not establish the diagnosis beyond question because the organism is known to occur in vegetable material and has been isolated from the mouths of apparently normal *animals If the patient's* serum contains agglutinins for the spores of the *Sporotrichum* of his own culture in a dilution of 1 50 as a minimum or up to 1 1000 or above, the diagnosis is a little more likely Such patients should be treated intensively with iodides on the assumption that sporotrichosis *is the correct diagnosis*

Sporotrichosis must be differentiated from syphilis, tuberculosis, pyogenic infections, glanders, leprosy, tularemia and other type of mycoses

The prognosis is excellent in the lymphatic type but poor with the visceral and pulmonic forms

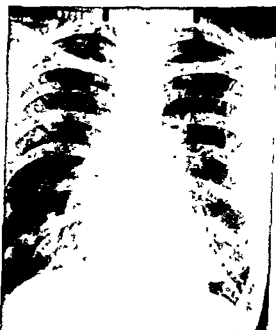


Fig 12 Sporotrichosis of the lungs, showing diffuse small nodular shadows throughout both lungs with some involvement of the hilar lymph nodes The lesions disappeared *following potassium iodide therapy (After Moore and Kile Arch Dermat & Syph, 31* 672, 1935)

Potassium iodide is practically a specific in the treatment of sporotrichosis *The initial* dose may be 10 drops of a saturated solution t i d p c diluted in water or *milk*, and may be increased by 3 to 5 drops with each of the three *daily doses* To avoid recurrences, the treatment should be continued for four to six weeks after apparently complete recovery Open lesions may be compressed with Lugol's

solution X ray therapy is indicated as a supplementary treatment for particularly indolent lesions Vaccine therapy for desensitization may be tried if the response to iodides is unsatisfactory and if this fails a course of hydroxystilbamidine should be tried

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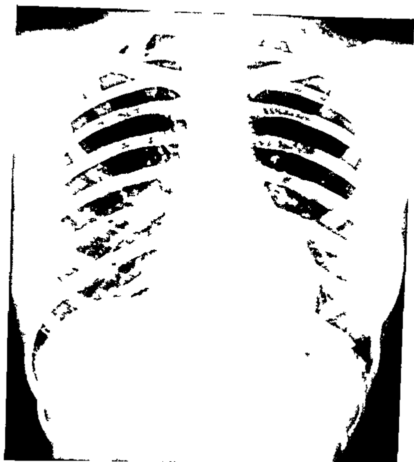


Fig 13 Histoplasmosis showing calcification in lung fields and in hilar lymph nodes This film was from a healthy student nurse who had a negative tuberculin and a positive skin test to histoplasmin (Courtesy of Dr C E Palmer after Smith *Clinics* 4 1025 1945)

A *localized primary pulmonary infection* is very difficult to differentiate from an asymptomatic or mild primary infection with tubercle bacilli In both instances the organisms are breathed into a localized area of the lung proceed to multiply and produce an expanding area of pneumonitis The organisms drain into and enlarge the regional lymph nodes The peripheral lung lesion begins to retrogress after a few weeks although the hilar nodes may continue to enlarge for some months After 4 to 12 months the peripheral lesion is reduced to a few rather small dense areas and after 3 to 5 years these areas appear calcified At the same time varying amounts *of calcium is found in the regional lymph* nodes Small localized infections rarely stimulate the production of detectable complement fixing antibodies to histoplasmin or yeast phase antigen or the stimulation is transient and has disappeared before the patient is studied The histoplasmin skin test which is negative before infection becomes positive after 2 to 3 weeks and persists for years if not for life A single peripheral pulmonary lesion before calcification may simulate the coin" lesion of an early neoplasm

Diffuse primary pulmonary infections presumably result from a massive inhalation of infecting tuberculate spores Small "cotton ball" or "snow flake like lesions are rather evenly distributed throughout both lungs This form of the disease is readily differentiated from primary tuberculosis but can be duplicated by primary coccidioidomycosis or Q fever These patients are often ill and sometimes severely ill for weeks or months The skin test becomes positive after 2 or 3 weeks *Complement fixing* antibodies are usually present in the serum after 3 to 4 weeks but disappear after 4 to 6 months with the clearing of the peripheral lesions In some instances the small peripheral lesions apparently disappear completely after a year but a non visible residue is left which is quite obvious 3 to 5 years later when a hundred or

more calcified lesions are found by x ray Needless to say there is every conceivable gradation between the localized primary and the diffuse primary infection Occasionally even the *diffuse primary lesions may run their* course without recognizable symptoms We have seen a dental student who had a normal x ray in January a very brief but definite exposure to dust from a chicken house in March and an x ray in August which showed the lungs *filled with small "snow flake" lesions* He was under close medical supervision and had no symptoms at any time His allergy was of a low degree and a 1 10 dilution of histoplasmin was required to give a positive skin test This *may or may not have been responsible for his* lack of symptoms

Localized mucosal or intestinal infection may result from local infections in the ears nose pharynx larynx lip penis or in the mucosa of the intestinal tract The intestinal ulcerations are apparently limited to young children and are associated with marked splenomegaly and hepatomegaly marked mesenteric adenitis moderate generalized lymph node enlargement and minimal late pulmonary lesions With the exception of the intestinal ulceration the other localized infections may at times be local manifestations of a systemic invasion as suggested by Loosh The prognosis is grave in these types of "local lesion" whether primary or secondary in contrast to the massive diffuse primary pulmonary infection where the prognosis is excellent

The *disseminated primary infection* has a high mortality and there seems to be no quantitative relationship between the extent of the primary pulmonary infection and the amount of dissemination Small pulmonary lesions may be followed by marked infection of liver spleen suprarenal bone marrow and other organs In rare instances the organisms may settle on the heart valves giving an endocarditis or in the brain to give a meningitis One is tempted to suggest that there is some defect in the immune mechanism of these patients which deprives them of the normal expected amount of resistance These patients may run their course to death without ever developing a positive histoplasmin test and if once positive it later became negative Loosh has found that complement fixing antibodies are usually present during the course of the disease but may be negative in the terminal phases of infection and also in the terminal phase of infection with secondary mucosal and skin lesions

Subacute primary infections are not common but are being recognized with greater frequency as groups of patients are studied with more care Patients with a few or a number of primary foci respond in the usual manner to rest therapy with the disappearance of symptoms and almost but not complete disappearance of the pulmonary lesions The complement fixing antibodies progressively decrease to a low titer Some weeks or months after resuming full activity symptoms recur the almost healed lesions in the lungs enlarge in size and the complement fixing titers are again elevated They respond again to rest treatment but may again relapse with activity Several patients with this type of disease have been studied by White and Hill and by Lehan and Furcolow

Epidemic histoplasmosis masqueraded under a variety of names such as "cave sickness" "acute miliary pneumonitis" or "primary atypical pneumonia" until the studies of Loosh at the "Silo" epidemic and the more extensive studies of Furcolow and his associates showed that these epidemics were indeed caused by *Histoplasma capsulatum* Lehan and Furcolow collected and reported in 1957 on 41 such epidemics which involved 400 individuals They occurred in both endemic and nonendemic areas Four such epidemics have been recognized in South Africa and one each in Peru and Venezuela There were 5 deaths 4 of which were in children The incubation period may be as short as 7 days but is usually about 14 days The patient may have the most fever and the most dyspnea shortly after the histoplasmin test becomes positive There is no significant difference between the epidemic form of the disease and the diffuse primary infection described above in the sporadic infections except certain of these patients have extraordinary massive infections There is a rough correlation between the amount of exposure in a group of individuals and the extent of the pulmonary infections (Fig 11)

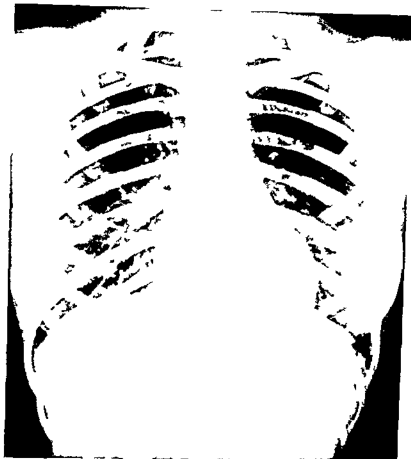


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tions the test with the histoplasmin antigen may be positive when the yeast phase antigen is negative. The serology of histoplasmosis is not as well standardized as that of coccidioidomycosis varying with the laboratory performing the test as well as with the type of antigen employed. Cross reactions with the *Blastomyces* antigen are frequently encountered and both antigens should be used when either histoplasmosis or blastomycosis is suspected. Cross reactions with coccidioidin are unusual.

The *colloid agglutination test* which is a modified precipitin test is quite sensitive and can be used to eliminate antibodies to either histoplasmosis or blastomycosis but cannot be depended upon to differentiate between the two infections.

Treatment of a specific nature is not needed for the milder infections. There were only 5 deaths among the 400 patients involved in the histoplasmosis epidemics although many appeared critically ill for weeks. A specific treatment is needed for the infections in young children in disseminated infections in ulcerative mucosal cutaneous and intestinal infections and in fibrocavitary reinfection histoplasmosis. Three new drugs are being investigated but none have been critically evaluated. Two are chemotherapeutic drugs and one is an antibiotic. The first is *ethyl fincolate* (MRD 112) which is entirely harmless in therapeutic doses and has shown some promise in acute disseminated infections. It was a definite failure however in fibrocaseous cavitary cases. The second is a *bistertiary amine* which has some therapeutic effect. The third and most promising is the antibiotic *Amphotericin B*. This has produced improvement in cavitary cases progressive infections and in one case of chronic meningitis. The value and limitation of this antibiotic will probably be in the literature by the time this book is published.

ASPERGILLOSIS

There are many species of *Aspergillus* and a few of these such as *A fumigatus* *A clavatus* *A niger* and *A versicolor* can under exceptional conditions produce disease in man. It is difficult to establish a diagnosis without a biopsy of the lung since *aspergilli* are ubiquitous and the spores may be inhaled one day and recovered in a culture of sputum or bronchoscopic drainage the next day without ever having infected the lungs. If hyphae forms of the organism are found in freshly expectorated sputum one can conclude that the fungus is growing in the bronchi or lungs but it may be a secondary invader and not the cause of the disease.

The hyphae forms of the organisms grow in the lungs but diagnostic spore heads are never formed unless the hyphae forms reach air in a bronchus or in a cavity.

Aspergilli may produce inflammation granulomatous lesions in the skin external ear nasal sinuses orbit etc bones meninges and lungs. Three clinical types of pulmonary infections are known. The first presents no characteristic clinical or roentgenographic picture and is usually diagnosed at necropsy or after resection of an infected lobe. The second type of infection produces an allergic type of migrating pneumonitis sometime with but more often without an associated eosinophilia (Fig 15). The third type begins as a single area or multiple areas of diffuse pulmonary infiltration which over a period of weeks or months becomes sharply circumscribed extremely dense circular objects which resemble marbles or golf balls. Some excavate leaving thin walled cavities which persist for years (Fig 16).

The migrating pneumonitis type of infection should be treated with autogenous vaccines made from the fungus and any other aerobic or anaerobic organisms which can be cultured from the sputum. These patients always give an immediate type of 30 minute skin reaction but may give a delayed reaction also. The solid ball like lesions should be resected

Individuals who have positive skin tests may escape *infection or may have an infection* which begins earlier but runs a shorter and milder course The latter type of case has been observed by Lehan and Furcolow

Reinfection histoplasmosis can be separated *sharply from all the clinical types previously* described A period of years may elapse between the patient s primary symptomatic or more often asymptomatic infection and the development of reinfection histoplasmosis *This is shown by the presence of miliary calci*fied lesions scattered evenly throughout the periphera of the lungs at the time of onset of the unilateral or bilateral apical or subapical *lesions Not all of the lesions* are in the upper *lobes* but the proportion *is* is high as in reinfection pulmonary tuberculosis The first cases of this type were recognized by Johnson and Batson in 1948 and confirmed by Sutliff and Burkett The physical findings symptoms and x ray *shadows are identical with the* typical fibrocaseous cavitary tuberculosis Occasionally the patient is tuberculin negative and histoplasmin positive but more often both skin tests are positive The diagnosis is es*tablished by staining the organisms in cells* from the sputum or gastric washings or by cultures or sections of surgically removed specimens of the lung

Most of the patients eventually find their *way to a sanatorium for* tuberculosis and a number do have both tuberculosis and histoplasmosis The diagnostic problem which confronts the sanatorium physician was reviewed by Furcolow and Brasher in 1956 These authors suggest that there may be as many as 400 unrecognized cases of histoplasmosis or the combination of histoplasmosis and tuberculosis in sanatoriums which draw their patients from areas where 50 per cent of the population have positive histoplasmin skin tests The skin tests are practically always positive in these cases of rein*fection histoplasmosis and the complement* fixation tests are positive in the actively progressive cases The *prognosis* has been poor in reinfection histoplasmosis although some have been cured by surgical resection

The *histoplasmin skin test* usually becomes positive 2 to 3 weeks after infection and remains positive for many years However it may never develop in rapidly disseminating cases or if positive early may become negative in the terminal stage of the disease The usual dose is 0 1 ml of 1 100 dilution of histoplasmin which is injected intracutaneously like a tuberculin test and read after 24 48 and 72 hours The reaction usually reaches its maximum size at 72 hours Cross reactions are frequent with blastomycin and occasionally observed with coccidioidin No difficulty will be encountered if all three tests are performed simultaneously

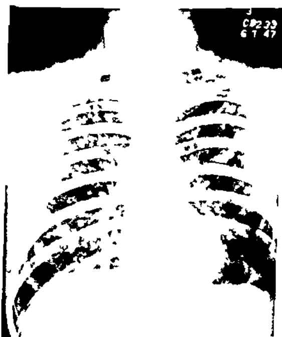


Fig 14 Acute epidemic histoplasmosis caused by inhalation of dry pigeon manure (From Parrott Taylor Poston and Smith *South M J* *48* 1147 1955)

The precipitin test begins to rise after 7 to 14 days and then starts to decline as the complement fixation test reaches its maximum after 3 to 4 weeks The precipitin test in histoplasmosis is not as reliable as the precipitin test in coccidioidomycosis The *complement fixation* test is performed with either a yeast phase antigen or with histoplasmin The antibodies *detected by the yeast* phase antigen appear somewhat earlier and reach higher titers than those detected with the histoplasmin antigen However in chronic infec-

tions the test with the histoplasmin antigen may be positive when the yeast phase antigen is negative. The serology of histoplasmosis is not as well standardized as that of coccidioidomycosis, varying with the laboratory performing the test as well as with the type of antigen employed. Cross reactions with the *Blastomyces* antigen are frequently encountered and both antigens should be used when either histoplasmosis or blastomycosis is suspected. Cross reactions with coccidioidin are unusual.

The *colloid agglutination test*, which is a modified precipitin test, is quite sensitive and can be used to eliminate antibodies to either histoplasmosis or blastomycosis but cannot be depended upon to differentiate between the two infections.

Treatment of a specific nature is not needed for the milder infections. There were only 5 deaths among the 400 patients involved in the histoplasmosis epidemics, although many appeared critically ill for weeks. A specific treatment is needed for the infections in young children, in disseminated infections, in ulcerative mucosal, cutaneous and intestinal infections and in fibrocavitary reinfection histoplasmosis. Three new drugs are being investigated, but none have been critically evaluated. Two are chemotherapeutic drugs and one is an antibiotic. The first is *ethyl fincolate* (MRD 112), which is entirely harmless in therapeutic doses and has shown some promise in acute disseminated infections. It was a definite failure, however, in fibrocaseous cavitary cases. The second is a *bistertiary amine* which has some therapeutic effect. The third and most promising is the antibiotic *Amphotericin B*. This has produced improvement in cavitary cases, progressive infections and in one case of chronic meningitis. The value and limitation of this antibiotic will probably be in the literature by the time this book is published.

ASPERGILLOSIS

There are many species of *Aspergillus* and a few of these, such as *A. fumigatus*, *A. clavatus*, *A. niger* and *A. versicolor*, can under exceptional conditions produce disease in man. It is difficult to establish a diagnosis without a biopsy of the lung, since *aspergilli* are ubiquitous and the spores may be inhaled one day and recovered in a culture of sputum or bronchoscopic drainage the next day without ever having infected the lungs. If hyphae forms of the organism are found in freshly expectorated sputum, one can conclude that the fungus is growing in the bronchi or lungs, but it may be a secondary invader and not the cause of the disease.

The hyphae forms of the organisms grow in the lungs, but diagnostic spore heads are never formed unless the hyphae forms reach air in a bronchus or in a cavity.

Aspergilli may produce inflammation granulomatous lesions in the skin, external ear, nasal sinuses, orbit, eye, bones, meninges and lungs. Three clinical types of pulmonary infections are known. The first presents no characteristic clinical or roentgenographic picture and is usually diagnosed at necropsy or after resection of an infected lobe. The second type of infection produces an allergic type of migrating pneumonitis, sometime with but more often without an associated eosinophilia (Fig. 15). The third type begins as a single area or multiple areas of diffuse pulmonary infiltration, which over a period of weeks or months becomes sharply circumscribed, extremely dense, circular objects which resemble marbles or golf balls. Some excavate, leaving thin-walled cavities, which persist for years (Fig. 16).

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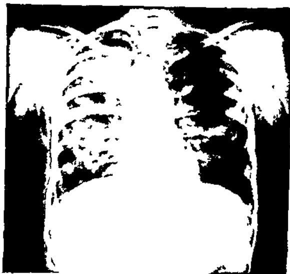


Fig 15 Aspergillosis of the lungs proved by repeated demonstrations of hyphal elements in the fresh sputum The patient gave an immediate wheal like reaction to a vaccine made from his own culture (Courtesy of Dr H A Bray New [illegible] Company 1944)



Fig 16 Aspergillosis of the lungs Note one *solid ball like lesion and one lesion containing air* This case was discovered in a naval hospital

PENICILLIOSIS

Penicilliosis is less frequent than aspergillosis The pulmonary lesions suggest an atypical pneumonitis, an organizing pneumonia, or a pulmonary abscess The diagnosis is made by finding the hyphae form in the fresh sputum and isolating the fungus from the same specimen or by pulmonary biopsy Treat*ment with vaccines should be tried if positive* skin tests are obtained with a vaccine made from the patient's own culture If improvement does not occur in 2 to 3 weeks a pulmonary resection should be advised

MUCORMYCOSIS

Mucormycosis may be caused by any one of the three genera, *Mucor, Absidia* or *Rhizopus*, which make up the order *Mucorales* The *infection occurs most often in patients with* uncontrolled diabetes leukemia or myeloma and in patients who have been treated with cortisone ACTH and other corticosteroid hormones, or broad spectrum antibiotics The *infections begin most often in the orbit or* sinuses but may start in the lungs or intestine The organisms grow in the walls of the blood vessels and cause death by metastases to the brain Wide, non septate hyphi, *6 μ to 50 μ in width, are found in the tissues* The genus and species cannot be established without a culture

The *diagnosis* should be established before *metastases have occurred in the brain* The diabetes should be controlled, the hormones or broad spectrum antibiotics discontinued to restore the patient's natural resistance Sinus infections and even lobes of the lungs (Fig 17) should be excised to prevent metastatic spread Harris has reported the cure of one case even though there was blindness in one eye and a partial paralysis at the time the *diagnosis was made* This patient had uncontrolled diabetes with an ulceration of the



Fig 17 Mucormycosis of the left lower lobe This case was discovered at necropsy (From Baker Am J Path 32 287 1956)

palate and infection of the left ethmoid and maxillary sinuses The diabetes was controlled local lesions drained and autogenous vaccines and iodides were administered

CONIOSPORIOSIS

A peculiar type of pneumonitis has been found in lumbermen in the northern forests who are exposed to the spores of *Coniosporium corticale* which grow on the inner bark of dead maple logs The primary inhalation causes no symptoms but after repeated inhalations 10 to 20 per cent of the lumbermen develop a pneumonic reaction in their lungs with severe constitutional symptoms The lesions disappear with rest in bed after three or four weeks The pneumonitis recurs when the patient again breathes in the spores This disease has been studied by Towey Sweany and Huron These investigators have reproduced the disease in guinea pigs by forcing the pigs to inhale the offending spores This seems to be an example of an allergic pneumonia and there is no evidence that the fungus actually grows in the pulmonary tissues

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CHAPTER 10

Hutchinson-Boeck Granulomatosis (Sarcoidosis)

J ARTHUR MYERS, M D

ALMOST two dozen names have been applied to this condition such as Hutchinson-Boeck's disease, Lymphogranulomatosis Benigna, Boeck's sarcoid, Besnier-Boeck's disease, and Besnier Boeck-Schaumann's disease Middleton says, "Until a better term is fixed by a clear definition of its order, the eponym Hutchinson Boeck granulomatosis would have the advantage of historical accuracy and sharper delimitation"

Apparently the first case was described in 1875 by Hutchinson The patient's name was Mortimer, so he named it Mortimer's malady Hutchinson had observed this patient for several years with nodular lesions on the arms, fingers, and legs The next case was described by Besnier in 1889 This patient's findings consisted of swelling of the interphalangial joints of the fingers, the ears and the nose Besnier called it lupus pernio Ten years later, Boeck described both the clinical manifestations and the microscopical findings of lesions obtained from skin which he thought resembled sarcoma and, therefore, he called it multiple benign sarcoids By 1905, he had studied ten cases which had shown a preponderance of lesions in the lymphatic system, the skin and the mucous membrane of the nose Another ten years of observation of patients and microscopical studies of their lesions had convinced him that the condition is a generalized one, and he believed it was caused by attenuated tubercle bacilli Therefore, he named it Benignes Miliar Lupoid

Lesions in the lungs were first described by Kuznitzky and Bittors in 1915 This patient also had lesions in lymph nodes, skin, and internal organs

Between 1919 and 1928, Jungling studied x-ray shadows of bones of a patient who revealed cyst-like x ray shadows Microscopical studies were made from a diseased finger which he thought was an unusual form of tuberculosis Before, during and after Jungling's observations, Schaumann made extensive studies and also thought it to be a tuberculous condition

In more recent years, numerous detailed studies have been made on this condition, and a large number of excellent articles have been published

PATHOLOGY

Cases have been described with only one or two small areas of disease while in others, numerous lesions have been found, in fact, in nearly every organ of the body This difference may be due in part to duration of the disease at the time it is first diagnosed Organs most frequently involved are lymph nodes, skin, lungs, eyes, spleen and liver Grossly the areas of disease range in size from small nodules to large, dense, areas throughout the lungs, extensive enlargement of the spleen, and massive lymph nodes Cut surfaces of lesions appear homogenous and are either firm or soft They are never purulent or caseous

Microscopically large tubercles composed of numerous epithelioid cells are found in the lesions Occasional multi-nucleated giant cells are present, but lymphocytic infiltration at the periphery is slight or absent Crystal appearing giant cell inclusion bodies known as Schau-

mann bodies are in evidence but they are not helpful in diagnosis as they are observed in lesions of other diseases including leprosy and sometimes tuberculosis

In the center of some of the tubercles there is evidence of necrosis but this does not change into granular caseation as occurs in tuberculous lesions In sarcoid tubercles the necrotic tissue becomes eosinophilic fibrous hyaline or fibrinoid substance

Even microscopically sarcoid epitheloid tubercles cannot be differentiated from those seen in such conditions as brucellosis beryllium granulomatosis certain fungus diseases leishmaniasis leprosy syphilis tuberculosis and tularemia

ETIOLOGY

Sarcoidosis is still thought by many physicians to be an infectious process However microscopical studies have not yet revealed bacteria or fungi that might be responsible Moreover cultures of entire involved lymph nodes and inoculation of materials from sarcoid lesions in guinea pigs hamsters rabbits mice chickens pigeons and ducks have failed to demonstrate the etiological agent

Middleton says "In spite of extended studies the etiology of Hutchinson Boeck granulomatosis remains an enigma Although its cause has escaped detection, the evidence of its independent order is growing In spite of indubitable histologic parallelisms the responsibility of known bacterial infections as tuberculosis leprosy and brucellosis fungus invasions as histoplasmosis and toxoplasmosis infestations as leishmaniasis and helminthiasis and particulate matter as talc silica dioxide and beryllium phosphors for this widespread reaction has largely been dispelled"

INCIDENCE

Until recently so many diagnoses of sarcoidosis were made without adequate documentation that incidence figures were unreliable However with more complete examination leading to accuracy of diagnosis the incidence is better understood

During World War II among 297 cases of proved sarcoidosis among military personnel it was observed that the attack rate was 6 3 per 100 000 among those from the South Atlantic Gulf Coast states 1 5 among those from the Middle Atlantic and Border states and only 0 7 per 100 000 from the rest of the United States A preponderance of the cases came from rural areas Among those from the South Atlantic Gulf Coast states the ratio of Negroes to caucasians was 18 to 1 from the Middle Atlantic and Border states it was 22 to 1 and from the rest of the country 17 to 1 Reports from various parts of the world indicate that sarcoidosis is widespread

Judging from accounts in the world s literature the chief foci seem to be in the British Isles France Germany Scandinavia Switzerland and the United States It is primarily a disease of young adults although it has been reported in persons of all ages Apparently it occurs about equally in women and men

In Denmark and in the vicinity of Baltimore the majority of the patients resided on farms or in villages Some evidence has accrued to suggest a familial factor At least three pairs of identical twins have been reported as well as families in which several members developed this condition

CLINICAL FEATURES

Although the occasional case may have body temperature from 101 to 103°F for a few weeks in the majority fever has not been reported Now and then an individual appears chronically ill but most patients are in reasonably good general health This observation may be due in part to the stage of the disease present when first examined and to relatively short periods of observation thereafter

SKIN

In approximately 1 in 4 cases small to medium sized and sometimes large usually firm and deeply placed nodules or plaques of semi translucent waxy appearance occur in the skin There is no evidence of inflammation or tenderness and ulceration almost never appears They are sparsely distributed over all parts of the body After first being observed they have been reported to progress or regress They may almost completely disappear at least temporarily They are differentiated histologically from tuberculosis with difficulty



Fig 1 This man of 45 developed a chest cold in March 1952 X ray film revealed slight enlargement of hilum region right side which was larger in April when the left hilum was also en

1956)

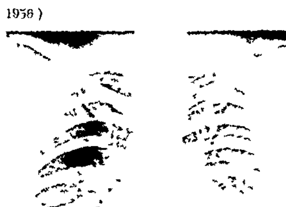


Fig 2 From a roentgenogram taken routinely May 2 1954 of the chest of a man of 29 years No symptom no evidence of significant disease

EYE

A considerable percentage of cases have involvement of the eye This has been observed up to 65% Persons with pulmonary involvement seem to have ocular lesions more frequently than others A number of cases have been reported with eye symptoms as the first manifestation of the disease The uveal tract is more often involved than the adnexa

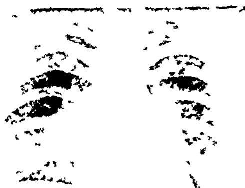


Fig 3 From a roentgenogram taken September 1 1955 of same chest seen in Figure 2 Note marked enlargement of hilum shadows No symptom

In about 15% of cases lesions appear in the sinuses tonsils and nose even to the point of causing nasal obstruction

Lymph nodes are nearly always involved This applies to both superficial and deep nodes (Fig 1 2, 3) The condition when first found may be limited to a single or a small group of nodes In other cases general enlargement of nodes is observed

PAROTID GLANDS

Sarcoidosis involves one or both parotid glands with considerable frequency. Enlargement of these glands may coexist with lesions of the lachrymal or uveal tract with transitory facial nerve paralysis. It is now believed that uveoparotid fever is not an isolated disease entity but a manifestation of sarcoidosis.

LUNGS

In 80% or more of sarcoidosis cases lesions may exist in the lungs or mediastinal lymph nodes or both. In the lungs a single small area of involvement may cast an x ray shadow. At the opposite extreme numerous shadow casting lesions may be present throughout one or both lungs. Even in extensive lung involvement there is usually a sparsity of symptoms, such as slight unproductive cough unless secondary bronchiectasis develops. Only extreme cases present evidence of respiratory embarrassment. The lack of or mildness of symptoms is probably due to only proliferative tissue reaction such as is seen in silicosis as well as the large pulmonary reserve that is the vital capacity of approximately eight times the tidal air in the normal person. Moreover pulmonary tissue is not supplied with sensory pain fibers.

It is impossible to differentiate sarcoidosis from many other conditions from the shadows lesions cast on x ray film. Those of sarcoidosis may appear identical to those of bronchiolitis, berylliosis, congestive failure, silicosis, carcinomatosis and diffuse interstitial fibrosis. Most every pulmonary shadow casting lesion of any disease including extensive consolidation and cavitation may be seen in cases of sarcoidosis. Spontaneous pneumothorax occasionally occurs. Sarcoid pulmonary lesions may change from time to time almost to the point of disappearing from x ray view only to recur later. This has caused confusion in diagnosis with lesions of Loeffler's syndrome.

HEART AND PERICARDIUM

In 10 to 20% of cases of sarcoidosis the heart is involved with different manifestations such as cardiac enlargement, bundle-branch block, complete heart block, extrasystoles and T wave changes. Sarcoid tissue may invade the pericardium. Riley reported right heart failure in 8% of his cases. This results from long standing extensive pulmonary disease just as it occurs in other conditions such as silicosis. Except for cases of cor pulmonale symptoms in cases of cardiac involvement are rare.

SPLEEN

Twenty per cent or more of persons with sarcoidosis have been found to have involvement of the spleen. This organ may become extremely large and splenic tissue may be almost completely replaced with sarcoid lesions.

LIVER

Twenty per cent or more cases of sarcoidosis also have hepatic lesions. This may result in moderate enlargement of the liver. Occasionally the bilirubin excretion test has revealed impairment of liver function. Jaundice occasionally occurs.

BONES

In 10 to 15% of persons with sarcoidosis changes are found particularly in bones of the hands and feet such as marked irregular enlargement of the phalanges resulting in disability and deformity. X ray film inspection may reveal large areas of rarefaction and irregular enlargement of the bones and sometimes small punched-out areas. Periosteum and joints are rarely involved except in occasional advanced cases.

NERVOUS SYSTEM

In the central nervous system sarcoidosis may result in encephalitis and meningitis. The pituitary gland has been found involved. Occasionally transitory facial paralysis occurs probably from pressure of enlarged parotid glands.

OTHER LOCATIONS

Although lesions *may occur in kidneys*, in about 5 per cent of cases, Longcope and Fisher did not find definite evidence of renal insufficiency *Voluntary muscles* have been *found to* contain masses of sarcoid lesions

DIAGNOSIS

Every person who receives the diagnosis of sarcoidosis should have the condition thoroughly documented No symptom, physical sign or x-ray shadow is pathognomonic There is no universally recognized specific test The most important evidence is enlargement of lymph nodes (Figs, 1, 2 and 3), presence of pulmonary and eye lesions, enlarged spleen, elevated serum globulin, cystic changes in the bones of the hands and feet Most important, are histological features of biopsy or postmortem lesions In cases of pulmonary involvement, if an enlarged superficial lymph node can be found, biopsy is indicated If no such node is available, scalene node biopsy (Fig 4) is often performed even though there is no demonstrable enlargement of such nodes Liver and spleen biopsies are occasionally done

Difficulty is encountered in the differential diagnosis with several other diseases, including pulmonary tuberculosis, carcinomatosis, syphilis, Hodgkin's disease, lymphosarcoma and follicular lymphoblastoma

LABORATORY AIDS

In approximately 50% of cases, elevated serum globulin has been reported The Kveim test is based on the phenomenon that emulsions from sarcoid lesions may produce sarcoid-like reaction in patients This test enjoys considerable usage, but some workers have concluded that it is not specific Others have found a high percentage of reactors There are those who think the reaction is probably due to an allergic phenomenon and that sarcoidosis induces a specific allergy or creates an increased capacity on the part of the skin to become sensitized by the injection of heat-sterilized suspension of sarcoid tissues Although several other tests have been offered, none has been generally accepted

Considerable controversy has been waged concerning the tuberculin test in this disease Failure to react to tuberculin has been thought by some physicians to be supporting evidence for sarcoidosis However, Longcope and Fisher found 32% of 79 cases reacted, and Riley reported 35% of his 52 cases as reactors to tuberculin Failure to react to tuberculin may have been over-stressed as a diagnostic point The rapidly-decreasing incidence of tuberculin reactors, particularly in the age groups where most sarcoidosis occurs, may be partially responsible Another possibility is that cases of sarcoidosis have been tested only with weak solutions of tuberculin Like other



Fig 4 Microscopic section from a scalene lymph node, same man as seen in Figure 3 *Microscopical diagnosis—Sarcoidosis*

groups of individuals some persons with well documented sarcoidosis have later developed clinical tuberculosis *and* reacted to tuberculin

TREATMENT

Sarcoidosis has such a marked tendency to undergo remission and spontaneous healing that difficulty in evaluating any form of treatment used to date is obvious

Nothing specific has been found *If the* individual is not ill only dietetic and hygienic regimen *are* employed For ill persons *methods of reducing symptoms and bed rest* are indicated However there is no evidence that bed rest influences development of pulmonary *fibrosis*

Inasmuch as some persons with sarcoidosis later develop pulmonary tuberculosis preventive *measures have been employed,* but apparently have not been effective Among Riley's 52 cases 13 later developed pulmonary tuberculosis Three had previously been on no bed rest five had had bed rest from 1 to 5 months and the remaining five for more than 5 and up to 29 months It appears therefore that bed rest does not prevent later development of pulmonary tuberculosis Probably one of the main reasons for some persons with sarcoidosis later developing pulmonary tuberculosis has been that they have been placed on bed rest in sanatoriums and hospitals for the tuberculous with long exposure to tubercle bacilli

Refvem cited a case of sarcoidosis who did not react to tuberculin over a period of 18 years He introduced 0 10 mg of Bacillus Calmette Guérin and at the end of 4 months *a severe reaction suddenly* appeared at the site of administration This resulted in necrosis and ulceration At this time the skin was slightly sensitive to tuberculin The sarcoid lesions were unaltered From this experience the author recommends that both tuberculin negative and positive sarcoid patients be protected against exposure to tubercle bacilli

Sulfonamides and antibiotics apparently are of no avail

Shulman *et al* administered courses of ACTH or cortisone to 15 patients The active *disease regressed but there was no response* in long standing cases with extensive fibrotic changes After treatment was discontinued *some patients had prolonged remissions* Others promptly relapsed In others, some manifestations were suppressed while others *reactivated* In eight cases with acute uveitis the condition subsided but vision was restored only in those in whom uveitis had recently appeared The tendency toward relapse was great Skin and subcutaneous manifestations cleared in 9 of 10 persons but gradually reappeared in 5 of them Mediastinal lymph nodes decreased in size in 10 of 12 cases but relapse occurred in 8 None of his cases developed tuberculosis during treatment or as long after as the observation was continued

Those who still believe that sarcoidosis represents a response to an infection recommend that early detection and prompt treatment with various antimicrobial drugs is the best approach not only from the *standpoint* of altering the course *of* the disease but also possibly to aid in the clarification of its etiology

Hoyle *et al* treated 30 cases with streptomycin and para aminosalicylic acid and also with cortisone in 20 of them Improvement was rarely noticed in persons in whom the disease was known to have been present more than 2 years (1 in 9) whereas those with a shorter history improved (11 in 21) After treatment 11 relapsed completely and 4 partially The authors reported that prolonged administration of those drugs up to a year was safe and effective

PROGNOSIS

Earlier reports indicated that the prognosis is usually good However when individuals were observed over longer periods optimism was somewhat dampened Like any other



Fig 5 From a roentgenogram taken November 1954 of the chest of a woman of 21 years Note evidence of extensive bilateral disease Histological diagnosis of sarcoidosis about 3 years before and ACTH administered Temporarily improved Now has exacerbation (Myers Boynton and Diehl *Journal Lancet* April 1957)

chronic disease prognosis in sarcoidosis will not be known until a large number of cases have been followed for the remainder of their lives The longer persons with this condition have been followed the more apparent has become the seriousness of the disease Recurrence and late complications and ultimate deaths are more frequent than brief periods of observation indicated

It is a disease of remissions and exacerbations One or a group of lesions may be clearing while others are evolving in different areas

Some of the most serious complications occur in ocular sarcoidosis such as phthisis bulbi (shrinkage of the eyeball) ulcers of the cornea lesions of the uveal tract resulting in impaired vision and even blindness

Among 54 cases Fagerberg observed 5 with involvement of the lungs or eyes which resulted in severe invalidism Thirty two others had definite impairment of health Subjective and objective recovery occurred in only 10 However, these have not been followed to the end of life He believes sarcoidosis should never be considered a benign condition

In 25% of Riley s cases pulmonary tuberculosis developed It was chronic and protracted in most cases but in a few it was rapidly progressive

Prognosis must be especially guarded when the disease extensively involves the lungs (Fig 5) and tends to progress with deposition of fibroid tissue and cavity formation This also applies when the nervous system and the heart are involved Longcope and Fisher reported 6 3% deaths among 94 cases and among Riley s 54 cases the related mortality was approximately 20%

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CHAPTER 11

Pulmonary Abscess

J Arthur Myers M D

An area of local suppuration involving lung tissue is known as *pulmonary abscess* Such lesions vary from a few millimeters to ten or more centimeters in diameter While they are more frequently seen in the bases they may occur single or multiple in any part of the lungs Overholt et al designates as simple abscesses those with single or multilocular cavitation without secondary bronchiectasis and of less than 6 weeks duration Complicated abscesses consist of multiple isolated daughter lesions located in surrounding zones of pneumonitis which do not connect with the primary cavity About half as many pulmonary abscesses develop in the lungs of women as in men and nearly one half occur between the ages of 20 and 40 years

ETIOLOGY

ASPIRATION

Normal bronchi and the trachea efficiently eliminate foreign materials that enter them by bronchial peristalsis action of cilia and cough Most particulate matter such as dusts in the inhaled air is prevented from entering the lungs by the defense mechanism Anything that suppresses cough markedly interferes with removal of foreign materials from the bronchi and trachea and thus they accumulate When ciliated epithelium is injured or destroyed the bronchi and trachea are not kept cleansed in the usual manner and therefore foreign materials are not well removed

Nearly a third of a century ago Lemon placed in the mouths of anesthetized animals various substances which could easily be traced if they entered the lower respiratory tract such as stain barium and iodized oil When the anesthetized animals were on planes inclined at various degrees but with the head elevated above the body, aspiration occurred regardless of whether the anesthesia was light or deep However, when the downward inclination was increased less and less aspiration occurred In the Trendelenberg position no aspirated material was found With light anesthesia so the animal struggled swallowed or vomited there was an increased amount of material aspirated From these experiments he was convinced that infections about the upper air passages and the mouth are an important consideration in all operations requiring general anesthesia

Lemon emphasized that while under anesthesia the cough reflex is so impaired that materials laden with pyogenic micro organisms freely enter the trachea bronchi and pass peripheral ward and may remain to produce pulmonary abscess Therefore he recommended the greatest of care with regard to position of body during surgical operations to prevent aspiration of infected material He also emphasized that the patient should be examined carefully for upper respiratory infections before operations are performed since emboli may be set free at the time of surgery Single abscesses not infrequently follow operations on the mouth or upper respiratory tract, such as extraction of teeth and tonsillectomy

Thus, since Lemon's contribution, it has been known that many pulmonary abscesses result from material aspirated from the mouth nose, and pharynx carrying pyogenic organisms into the lower respiratory tract, which is unable to cleanse itself in a normal way It is not only anesthesia during surgical operations, but a number of other conditions which depress cough and gag reflexes such as unconsciousness from any cause, including alcoholism, cerebral accident, epilepsy, diabetic coma, injuries to the head, uremia, etc etc Persons in such states require the posture that Lemon described

One must not overlook the fact that deep sleep particularly among elderly persons, and sedatives, may depress reflexes enough to prevent adequate cough to keep the trachea and bronchi free from aspirated materials Obviously, foci of infection permitted to exist in the tonsils paranasal sinuses, gums, teeth, etc provide rich sources of pyogenic organisms when aspirated into the trachea and bronchi while they are unable to defend themselves

Whether or not an abscess is putrid depends upon the responsible microorganisms Smith and others have pointed out that nonputrid abscesses are usually caused by organisms such as pneumococci, Staphylococcus aureus and streptococci, whereas, anaerobic organisms which normally inhabit the upper air passages of adults and are especially numerous in the presence of carious teeth gingivitis, pyorrhea and diseased tonsils cause putrid lung abscesses These consist of spirochetes, fusiform bacilli, vibros and various gram negative bacilli Apparently no one of these organisms produces abscess, but a combination of them acting in symbiosis is necessary Approximately one fourth of pulmonary abscesses are non putrid and result from Escherichia coli, Klebsiella pneumoniae (Friedlander's bacillus), Staphylococcus aureus, Pseudomonas aeruginosa, and the Clostridia organisms

The location of pulmonary abscesses depends largely upon the position of the person when aspirated material passes from the trachea to the bronchi If the individual is supine as the aspirated organisms pass along the posterial walls of the bronchi, the first bronchus encountered is to the apical division of the lower pulmonary lobe Material that does not enter this bronchus is likely to enter ramifications to the posterior basal pulmonary segments

When the individual is in the lateral decubitus position, organisms are most likely to enter the axillary portion of the upper lobe

BRONCHIAL OBSTRUCTIONS

Although cough and gag reflexes are not repressed and the ciliated epithelium is functioning normally, obstruction of a bronchus or one of its branches prevents adequate drainage of its ramifications Therefore, aspirated material may enter before the obstruction is complete and is not entirely removed When the lumen is completely occluded, atelectasis occurs, thus creating a favorable situation for proliferation of microorganisms that may cause abscess

Bronchial obstruction may result from extrinsic pressure, from adjacent tumors, large lymph nodes, etc Intrinsic obstruction may result from mucous plugs, bronchial adenoma, cacinoma, etc Also, aspirated foreign bodies may be responsible Pneumoliths resulting from tuberculosis, fungus infections, etc may erode through walls of bronchial ramifications and be aspirated peripherally so as to result in obstruction Vinson called attention to calcifications produced by first infection type of tuberculosis and tracheo bronchial lymph nodes which ulcerated into bronchi and were aspirated so as to obstruct bronchial lumina

Bronchial obstructions, whether from extrinsic or intrinsic factors, are usually only partial in the beginning A check valve may result so air enters but is not expelled from the part of the lung supplied by the involved bronchus In such cases, localized emphysema, demonstrated by x ray film, may be the first manifestation of the presence of obstruction If the partial obstruction is due to bronchogenic carcinoma or aspirated foreign body, the carcinoma may gradually increase until the obstruction is complete While around the foreign body, sufficient reaction occurs to result in occlusion Whatever, the cause, after the bronchus is completely obstructed the trapped

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Whether or not an abscess is putrid depends upon the responsible microorganisms Smith and others have pointed out that nonputrid abscesses are usually caused by organisms such as pneumococci, Staphylococcus aureus and streptococci, whereas, anaerobic organisms which normally inhabit the upper air passages of adults and are especially numerous in the presence of carious teeth, gingivitis, pyorrhea and diseased tonsils cause putrid lung abscesses These consist of spirochetes, fusiform bacilli, vibros and various gram negative bacilli Apparently no one of these organisms produces abscess but a combination of them acting in symbiosis is necessary Approximately one fourth of pulmonary abscesses are non putrid and result from Escherichia coli, Klebsiella pneumoniae (Friedlander's bacillus), Staphylococcus aureus, Pseudomonas aeruginosa, and the Clostridia organisms

The location of pulmonary abscesses depends largely upon the position of the person when aspirated material passes from the trachea to the bronchi If the individual is supine as the aspirated organisms pass along the posterial walls of the bronchi, the first bronchus encountered is to the apical division of the lower pulmonary lobe Material that does not enter this bronchus is likely to enter ramifications to the posterior basal pulmonary segments

When the individual is in the lateral decubitus position, organisms are most likely to enter the axillary portion of the upper lobe

BRONCHIAL OBSTRUCTIONS

Although cough and gag reflexes are not repressed and the ciliated epithelium is functioning normally, obstruction of a bronchus or one of its branches prevents adequate drainage of its ramifications Therefore, aspirated material may enter before the obstruction is complete and is not entirely removed When the lumen is completely occluded, atelectasis occurs, thus creating a favorable situation for proliferation of microorganisms that may cause abscess

Bronchial obstruction may result from extrinsic pressure, from adjacent tumors, large lymph nodes, etc Intrinsic obstruction may result from mucous plugs, bronchial adenoma, cacinoma, etc Also, aspirated foreign bodies may be responsible Pneumoliths resulting from tuberculosis, fungus infections, etc may erode through walls of bronchial ramifications and be aspirated peripherally so as to result in obstruction Vinson called attention to calcifications produced by first-infection type of tuberculosis and tracheo bronchial lymph nodes which ulcerated into bronchi and were aspirated so as to obstruct bronchial lumina

Bronchial obstructions, whether from extrinsic or intrinsic factors, are usually only partial in the beginning. A check valve may result so air enters but is not expelled from the part of the lung supplied by the involved bronchus In such cases, localized emphysema, demonstrated by x ray film, may be the first manifestation of the presence of obstruction If the partial obstruction is due to bronchogenic carcinoma or aspirated foreign body, the carcinoma may gradually increase until the obstruction is complete While around the foreign body, sufficient reaction occurs to result in occlusion Whatever, the cause, after the bronchus is completely obstructed the trapped

CHAPTER 11

Pulmonary Abscess

J Arthur Myers M D

An area of local suppuration involving lung tissue is known as *pulmonary abscess* Such lesions vary from a few millimeters to ten or more centimeters in diameter While they are more frequently seen in the bases they may occur single or multiple in any part of the lungs Overholt et al designates as simple abscesses *those with single or multiocular cavitation without secondary bronchiectasis and of less than 6 weeks duration* Complicated abscesses consist of multiple, isolated daughter lesions located in surrounding zones of pneumonitis which do not connect with the primary cavity About half as many pulmonary abscesses *develop in the lungs of women as in men and nearly one-half occur between the ages of 20 and 40 years*

ETIOLOGY

ASPIRATION

Normal bronchi and the trachea efficiently eliminate foreign materials that enter them by bronchial peristalsis action of cilia and cough Most particulate matter such as dusts in the inhaled air *is prevented from entering the lungs by the defense mechanism Anything that suppresses* cough *markedly interferes* with removal of foreign materials from the bronchi and trachea and thus they accumulate When ciliated epithelium is injured or destroyed the bronchi and trachea are not kept cleansed in the usual manner and therefore foreign materials are not well removed

Nearly a third of a century ago Lemon *placed in the mouths of anesthetized animals various substances* which could easily be traced if they entered the lower respiratory tract such as stain barium and iodized oil When the anesthetized animals were on planes inclined at various degrees but with the head elevated above the body aspiration occurred regardless *of whether the anesthesia was* light or deep However when the downward inclination was increased less and less aspiration occurred In the Trendelenburg position *no aspirated material was found With* light *anesthesia so the animal struggled swallowed* or vomited there was an increased *amount of* material aspirated From these *experiments* he was convinced that infections about the upper air passages and the mouth are an important consideration in all operations requiring general anesthesia

Lemon emphasized that while under anesthesia *the cough reflex is so impaired* that materials laden *with pyogenic micro* organisms freely enter the *trachea bronchi and* pass peripheral ward and may *remain to produce* pulmonary abscess Therefore *he recommended* the greatest of care with regard *to position* of body during surgical operations *to* prevent aspiration of infected material He also emphasized that the patient should be examined carefully for upper respiratory infections before operations are performed since *emboli may be set free at the time of surgery Single abscesses not infrequently follow* operations *on the mouth or upper respiratory* tract such as *extraction of teeth and tonsillec*tomy

the cough usually increases Sudden expectoration of a large quantity—a half cupful or more of *fetid sputum* is not uncommon when an abscess ruptures into a ramification of a bronchus Pleural *pain* is a common symptom Abscesses following operations and aspirations from the mouth and throat usually have a sudden and severe onset Together with the above symptoms profuse sweating and prostration may occur On the other hand those which occur with slowly developing obstructions may have a more gradual onset with less severe initial symptoms such as *general aching* of the body and malaise *Blood spitting* varying in amount from streaks in the sputum to fatal hemorrhage may occur in pulmonary abscess

Multiple abscesses due to emboli from a suppurative condition elsewhere often have their symptoms masked by those of the other disease However one should always keep in mind this possible complication and if symptoms such as chest pain cough and expectoration appear multiple abscesses should be suspected Symptoms are not pathogonomic since all except the sudden expectoration of a large amount of fetid purulent material may be caused by other conditions and even this also occurs in empyema

EXAMINATION

If the abscess is small no abnormal sign is elicited by palpation percussion or auscultation As the area of disease increases in size and excavation occurs the usual physical signs appear as in any other condition resulting in infiltration consolidation and cavitation

On inspection the patient usually appears seriously ill Limited movement of the chest wall on respiration often occurs on the affected side and the phrenic wave sign is decreased or absent *Clubbing of the fingers and toes* sometimes occurs within a few weeks after onset of abscess *Hypertrophic pulmonary osteoarthropathy* develops in some cases These conditions may completely disappear when the abscess is brought under control at an early stage

X ray inspection both with the fluoroscope and the film is a valuable phase of the examination for determining the location and extent of gross disease Indeed in this manner one may locate lesions before other physical signs can be elicited On the other hand some abscesses are not located by x ray inspection Unfortunately, abscesses do not cast characteristic shadows However shadows may lead one to strongly suspect abscess but the cavitations consolidations infiltrations etc suggested by x ray shadows are no different than those produced by a number of other diseases Location of the lesion which casts the x ray shadow is not a safe criterion While it is true that many abscesses appear in the lower half of the lung they may and often do appear in the upper half

Bronchography may or may not be helpful even when cavitation exists Large cavities when completely filled with pus present no fluid level their outlines cannot be seen so their presence is not detected on the x ray film Even if a contrast medium is introduced in such cases it fails to enter cavities Therefore before attempting x ray inspection of the chest when cavities from any cause are suspected attempts should be made to have them evacuated through postural drainage etc If contrast medium can then enter and being heavier than pus it gravitates to the most dependent part of the cavity and if enough is introduced the pus which remains is evacuated after which the roentgenogram affords good evidence as to size and location of cavities The bronchogram is helpful in differentiating between bronchiectasis and abscess However coexistence of these conditions is not unusual

In observing the progress of abscesses the roentgenogram often reveals decrease or extension of areas of disease and changes in size of cavities before other phases of examination are of avail Therefore the x ray film should be used freely not only as an aid in diagnosis of abscess but also in observing its extension or retrogression

Bronchoscopic inspection should always be done when the attending physician is in doubt either as to the presence of abscess or its etiology The bronchoscopist aids greatly in locating an abscess by determining from which bronchus or ramification the pus appears The bronchoscopist s inspection may reveal evidence of obstruction If this is due to a for

air peripheral to it is absorbed and atelectasis is present It is not unusual for an area of atelectasis demonstrated on x ray film to be the first manifestation of total obstruction

OTHER CAUSES OF ABSCESS

Occasionally, abscesses follow *pneumonia* This may be due to bronchial obstruction resulting from mucous plugs, thus preventing drainage of the area Whether abscesses form in such situations is dependent upon microorganisms present Pneumococcic pneumonia probably never is followed by pulmonary abscess unless secondary invaders are present On the other hand, Klebsiella (Friedlander) pneumonia frequently results in pulmonary abscess

If emboli resulting in *infarction* are from septic thrombophlebitis or acute endocarditis on the right side of the heart, abscess frequently develops Even bland infarcts may result in pulmonary abscess if they become secondarily infected

Fungus infections, particularly actinomycosis, may be accompanied by pulmonary abscesses when secondary invaders are present

Penetrating infections from neighboring structures such as subdiaphragmatic abscess, mediastinitis, eophageal diverticulum and empyema may result in pulmonary abscess

Pulmonary abscess may occur in *tularemia*, *brucellosis* and *amebiasis* *Tuberculous* abscesses are not infrequent as the result of secondary invaders

Multiple abscesses may be due to emboli which arise from foci elsewhere, either in the presence or absence of surgery However, they occasionally follow broncho pneumonia. Meuwissen *et al* studied pulmonary changes in 14 persons with furunculosis Such changes were found in 9 Five of these complained of fatigue and cough The other 4 presented symptoms of septicemia Necropsy of 2 of these 4 cases revealed small, sub pleural staphylococcic abscesses, probably the result of hematogenous dissemination

Abscessed areas may be confluent or definitely separated from each other by normal lung tissue In fact, both lungs may be involved

Enlargement of abscesses occurs by direct extension or by spread of the infected material through the surrounding bronchi In the involved region the bronchi may dilate, after which it is impossible to determine whether the abscess or bronchiectasis was the original condition

Some workers believe that pulmonary *gangrene* is a separate disease entity and regard those caused by fusiform bacilli, spirochetes, etc, with fetid sputum, as gangrene, while those infected with other organisms are considered as abscesses However, it appears that abscess and gangrene merely represent various degrees of the same disease For example, if a large amount of abscess material is carried to other parts of the lung, gangrenous pneumonia may result

DIAGNOSIS

HISTORY

A recent attack of pneumonia or surgery, particularly of the mouth, nose or throat is significant Abscesses sometimes follow surgery of other parts of the body Pulmonary infarcts which develop, especially following operations on the pelvis, may lead to abscess formation History of an attack of choking while swallowing food or an attack of cough following aspiration of some other object is significant from the standpoint of foreign body abscess A period of unconsciousness from any cause is important particularly when accompanied by vomiting In some cases there is no suggestive history This is particularly true of foreign body abscesses in children

SYMPTOMS

A *chill* followed by fever similar to that seen in pneumonia may be the first manifestation of pulmonary abscess In the early stage of the disease *cough* and expectoration are slight or entirely absent As the condition progresses,

therapeutic reasons The needle may cause rupture of the abscess into the free plural space or this space may be contaminated as the needle is withdrawn with resulting mixed infection empyema Accidental pneumothorax may also be produced by leakage of air through the needle tract from the lung into the pleural cavity Manipulation of the needle sometimes causes hemorrhage air embolism or spread of the disease Moreover it is impossible to adequately drain an abscess through a needle as its contents consist of necrotic tissue clots and thick pus

As soon as abscess formation is in evidence the etiological agent should be sought in the laboratory since specific drugs are now available for a number of abscess producing organisms In the early course of the disease bacteriological determination may be impossible because of lack of sputum During this early acute stage crystalline penicillin G in water is administered intramuscularly in 500 000 unit doses every 6 hours Simultaneously every 12 hours 1 to 2 million units of penicillin in 10 cc of saline is administered intravenously

Penicillin administration may be supplemented by inhalation of neomycin in a solution of 0 5 gm in 2 cc of saline every 6 hours

When a mixture of micro organisms is demonstrated dihydrostreptomycin or streptomycin or aureomycin may be added to the penicillin treatment

When Endamoeba histolytica is the cause emetine hydrochloride (1 grain intramuscularly daily for 8 days) should be administered Nearly all patients recover on this treatment as shown by Ochsner *et al* This drug may cause muscle weakness myocardial damage necrosis and nausea Although the above dosage rarely does harm some physicians prefer chloroquine diphosphate in 0 25 gm tablets Four such tablets are administered at bedtime for 2 days then 2 tablets for 18 days A subsequent course may be given consisting of 2 tablets at bedtime for 10 days

For abscesses due to Klebsiella (Friedlander) pneumoniae chloramphenicol (*chloromycetin*) is the most useful present drug In severe cases 1 to 1 5 gm may be administered orally every 6 hours

When abscess is caused by Actinomyces israeli penicillin should be administered in large doses of 600 000 units intramuscularly every 6 hours This should be continued for 2 to 6 weeks In severe cases 10 000 000 or more units daily may be administered

When caused by Brucella abortus the best known drug treatment consists of 0 5 gm of streptomycin or dihydrostreptomycin every 12 hours for 2 weeks and 0 5 gm of aureomycin or terramycin every 6 hours for 3 weeks

Tularemic pulmonary abscesses respond best to 0 5 gm of streptomycin or dihydrostreptomycin divided into three equal doses and administered every 8 hours for 1 week If the patient is comatose the same dosage per day should be administered by continuous slow intravenous infusions

When pulmonary abscess is diagnosed early and specific drugs administered promptly excellent response occurs in many cases so that further treatment is not required However many cases are not seen by physicians until the abscesses are large or rupture has occurred The above drugs are also indicated in such cases but other measures are often necessary

POSTURAL DRAINAGE

After rupture has occurred and while patients are cyanotic have high fever rapid pulse low vital capacity and marked prostration *attempts at postural drainage are dangerous* Indeed they may prove fatal In the absence of severe symptoms however postural drainage is a distinct aid The position often advised for postural drainage with the head over the edge of the bed almost straight down from the hips is usually satisfactory for abscesses located in the basal segments of the lower lobes However this position is of no avail for most other abscesses Those in the upper lobes usually drain best when the patient is upright

The prone position is best for abscesses in the dorsal division of the lower lobe For those in the middle lobe and lingula the lateral decubitus position is best with the side of the abscess uppermost

It is usually best to have the patient find the position that causes most coughing as this provides for drainage regardless of position of

eign body, it may be removed If due to some other cause a piece of the tissue may be procured for microscopical inspection Not infrequently malignancy is first detected in this manner Again, pus may be aspirated for bacteriological and cytological study and contrast medium introduced so satisfactory bronchograms are obtainable Many abscesses are first diagnosed as pneumonia because of the similarity of symptoms Atelectasis due to bronchial obstruction casts a dense homogenous shadow which may not differ significantly from that cast by pneumonia If the bronchoscopist is called as soon as abscess is suspected, the removal of obstruction in some cases will establish free drainage and thus control the atelectasis and markedly reduce the potentialities of the abscess Coryllos found that even if the condition is finally diagnosed as lobar pneumonia, no harm has been done by bronchoscopy

Microscopical inspection is the last court of appeal with reference to etiology in many cases of pulmonary abscess It is only through this phase of the examination termine with accuracy the p in tissue removed by the br malignant cells in materi aspirated by the broncho bacteria, such as spirochet Klebsiella (Friedlander) p lococci, streptococci, pne roids, B pyocyaneus, H may be seen E coli and occasionally been found may occur in tularemi biasis Therefore these be kept in mind when t the etiological agent sis may coexist with disease, a search shoul tubercle bacilli

Some of the more must be considered in are empyema wit bronchietasis, cystic pulmonary tubercul

TREATMENT

GENERAL CARE

In any disease such as single pulmonary abscess, from which 25 to 30% of the patients recover spontaneously or with ordinary medical care, the physician should use extreme caution in evaluating any form of treatment Unless definitely more than 25 to 30% recover, the treatment administered has accomplished no more than would have been done by nature If this fact is constantly kept in mind therapeutic fads will be avoided On the other hand, the fact that 25 to 30% do come under control spontaneously or with ordinary medical care must not mislead the physician into procrastination The individual patient is more likely to belong to the 70 or 75% whose disease requires special therapy including surgical procedures if good results are to be accomplished

In single abscesses 10 to 14 days usually pass after the onset of symptoms before spontaneous rupture into bronchi occurs During this time and immediately after, *bed rest* is indicated with mild sed essary to insure rel and pain Howe be abolished Th best when maint proximately 68 to ity of about 40% tion and as free fr

Light but nour number of calori Stimulation of the of drugs to control portant Blood tran As in cases of pneu given on the appear the abscess is acute, o paralytic ileus

ASPIRATION CO

One should never attemp monary abscess by intr through the chest wall eith

ment has been too conservative and the surgeon has not been called sufficiently early Spontaneous recovery rarely occurs if the disease is allowed to persist more than a few weeks Therefore surgical consultation as soon as the diagnosis is made may markedly improve prognosis in a high percentage of those in whom it would otherwise be bad For example among 205 cases reported by Brunn 133 were treated medically at home Thirty one per cent improved and 35% died The remaining 34% were not referred to surgeons until an average of 460 days after the disease was first diagnosed Of the remaining patients in this group 72 were treated surgically of whom 56% improved Even in these improved cases surgery was not instituted until 451 days after symptoms first appeared Forty four per cent of these 72 patients died but surgery was not begun until 516 days after the disease appeared

In Overholt s series of 28 patients with complicated pulmonary abscess treated by external drainage the operative mortality rate was 32% and the cure rate was 26% In a series of 30 patients with simple pulmonary abscess the operative mortality rate was only 6% and the cure rate was 94%

Therefore modern treatment has markedly improved prognosis Murphy and Wolcott have reported 65 cases of pulmonary abscesses which they divided into three groups "The sulfonamide period 1941–1944 19 cases the penicillin period 1944–1952 29 cases the antibiotic or tryptar period 1952–1956 17 cases Mortality has fallen progressively from 31 5% in the first group to 17 2% in the second group to zero in the latest group They believe that factors which contributed to the lowered mortality were earlier institution of treatment and a larger number of effective drugs having become available Chemical debridement with tryptar was considered very useful

"Resection has replaced drainage procedures when surgery is needed Surgical management has been increasingly less needed in each group so that in the most recent series 65% required no surgery for cure"

PREVENTION

During the past 20 years the incidence of pulmonary abscess has markedly decreased No doubt the preventive measures practiced have had much to do with this situation and still more should be accomplished through them The following preventive measures are important

ORAL HYGIENE

Children develop pulmonary abscess and gangrene much less frequently than adults Probably this is because it is not until adulthood that the mouth becomes extensively contaminated with organisms capable of producing abscess through such conditions as pyorrhea and other foci of infection Moreover a greater number of abscesses appear in the lungs of men than in women which may be due in part to the fact that men have usually practiced much poorer oral hygiene than women The campaign of dentists for better oral hygiene has probably borne fruit in the reduction of the incidence of pulmonary abscess

PREPARATION FOR SURGERY

Surgeons of today see to it that their patients are rendered as free as possible from pathogenic microorganisms before surgery is undertaken that is they like to have such conditions as pyorrhea and other foci of infection about the mouth nose and throat brought under control before surgery is performed Even when such precautions are taken they prefer to use local anesthesia so as not to interfere with the cough reflex When general anesthesia is employed whether or not there has been time to attend to the oral hygiene the surgeon insists that the position of the patient s head and neck be at such a low level that there is no possibility of materials from the mouth and throat being aspirated into the trachea The

routine administration of antimicrobial drugs before and after surgical procedures apparently has prevented pulmonary abscess in many cases

Hyperventilation of the lungs following surgery, with insistence that the patient cough and expectorate, does much to maintain good drainage The surgeon should never be denied the opportunity of having the lungs carefully examined during the first few days or weeks following every operation

Bronchoscopic examination should be made immediately following suspected aspiration of foreign material which, if allowed to remain in the bronchi, may lead to abscess Therefore, any severe paroxysm of cough which cannot be explained on another basis should lead one to suspect aspiration Following pneumonia, the lungs should be examined with great care Failure of resolution at the proper time or the appearance of areas of atelectasis indicate immediate bronchoscopy At this time the removal of obstructive materials, such as mucous plugs, may prevent pulmonary abscess

Individuals unconscious from alcohol, narcotics or any other cause should immediately have the head and neck placed at such a low level that there is no danger of aspiration from the mouth and throat Elderly persons may aspirate materials during sleep Therefore, in addition to the practice of good oral hygiene they should sleep with the foot of the bed elevated

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CHAPTER 12

Bronchial Asthma

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DEFINITION

Bronchial asthma is an allergic condition, often hereditary, occurring at all ages and characterized by wheezing, dyspnea, orthopnea and cough. It is usually associated with rhinitis and is characterized by partial obstruction of the lower air passages.

ETIOLOGY

There are three basic factors to the asthmatic attack.[1] These are:

I. THE CONSTITUTIONAL BASIS

Heredity is important, with a positive family history of one or more allergic conditions in about 60% of cases. One inherits the predisposition to allergy but not necessarily the particular allergic disease; thus the grandfather may have asthma, the father hay fever and the grandson may have "eczema." Nor does one inherit the particular offending allergen, e.g., one member of the family may be allergic to fish, another to house dust and a third to ragweed pollen. The stronger the inheritance factor, the earlier, as a rule, is the onset of asthma; this is especially true in children. In instances of bilateral inheritance more than a third of the cases of asthma begin before the fifth year as contrasted with about 15% in the unilateral group and only about 5% in those with a negative family history. There is, however, no proof that infants are passively sensitized from the mother through the pla... ...ently sensitive to ...ich affect the ... after the age of 40, a history of allergy in the family is much less frequent and often entirely absent.

II. CONTRIBUTORY FACTORS

These are important but they rarely, if ever, initiate attacks of asthma. They may aggravate or incite attacks in allergic patients who are also exposed to various substances to which they happen to be sensitive. These contributing factors may be discussed under seven headings:

A. *Mechanical*, e.g., chalk and certain other dusts.

B. *Chemical*, e.g., fumes from tobacco, gasoline, molten metal, sulfur dioxide and turpentine. True allergy to tobacco probably occurs chiefly in those who work with the leaf. The detrimental influence of smogs as in Donora, Pennsylvania, and in London, England belong here. It is interesting to note that almost all the deaths and almost all the serious illnesses in these two disasters occurred in individuals who had either bronchial asthma or heart disease.

C. *Physical allergy*, e.g., light, heat, cold or pressure. Asthma from these exposures is very rare although they may cause urticarial lesions.

D. *Infections*, e.g., ordinary "colds," bronchitis and sinusitis. A "cold" should be defined as an acute contagious condition which usually begins with a raw throat, followed by

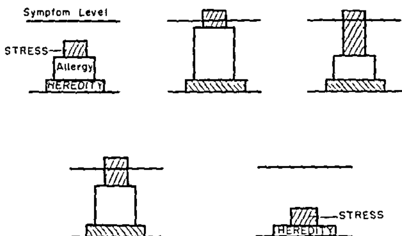


Fig 1 Relation of allergy and stress to asthmatic attacks (modified from Unger, A H and Unger, L *J Allergy, 23* 429-440, 1952)

acute rhinitis with blocking and a nasal discharge which contains many polymorphonuclear leucocytes Eosinophilia is usually absent from the nasal smear Fever is minimal and symptoms usually last about a week If asthma occurs, it usually begins about the second day, but, unless there is an inherited tendency to allergy, such "colds" rarely lead to true asthmatic attacks Non allergic members of the family may "catch the cold" but do not develop asthma

The above description of an infectious "cold" definitely separates it from allergic rhinitis which may come and go rather quickly or may persist for long periods, is not contagious, has no fever, and in such cases eosinophilia is usually present in the nasal smear

E *Psychogenic* Nervous and psychic factors are important predisposing causes, but we are confident that true bronchial asthma is not due solely to such stimuli As in the case of the other contributory factors, emotions can operate in patients who have a basic allergic condition (usually inherited), and who are also exposed to offending allergens

On the contrary, asthma itself is a frequent cause of nervousness The excitement of the attack, with its dyspnea, wheezing, cough and exhaustion, induces apprehension and irritability which are then aggravated by epinephrine and ephedrine used for treatment

We must make every effort to minimize emotional factors which can aggravate an attack Such emotions are common and important, and often precipitate an attack when all other conditions are constant This can be readily seen by examining Figure 1

F *Endocrine*, e g, puberty menstruation, menopause, pregnancy, are also important predisposing factors Asthma may be aggravated by approaching menstruation and lessened when the flow starts Pregnancy usually lessens asthma, although occasionally a patient will have asthma only during pregnancy The nervous factors incident to menopause seem to increase asthma in some women, but there is no proof that any endocrine influence alone can cause asthma Changes in adrenocortical function may be related to alterations in the allergic state in various endocrine situations

G *Miscellaneous* Exhaustion, constipation, poor hygiene and lowered morale should be combatted *An asthmatic patient is an individual who must receive general as well as specific treatment*

In summary, then, none of these contributory factors by themselves can initiate attacks of asthma or any other allergic condition They can however bring on or aggravate attacks in patients who are already allergic and

who are exposed to one or more of the allergenic substances now to be discussed

III. EXCITING FACTORS (ALLERGENS)

In the preceding sections the hereditary and contributory factors were discussed, and it was emphasized that neither of these can cause true asthma unless there is also exposure to one or more exciting substances, known as antigens, allergens or atopens

Most allergens contain protein, but certain non protein substances can cause attacks, e g, aspirin The carbohydrate fraction of a sub stance may be important, but the allergenic properties almost always lie in the protein fraction

The *allergic threshold* (Fig 1) or equilibrium is the barrier which prevents symptoms in sensitized persons Once this threshold has been overcome, as by exposure to an over whelming amount of ragweed pollen, symptoms occur It is difficult, if not impossible, to entirely restore this equilibrium, although injections of an extract of an offending substance constitute a step in this direction We therefore use the term "hyposensitization" rather than "desensitization"

There is a *time interval* between the first exposure to the specific allergen and the onset of symptoms When exposure is massive, as with workers in a bakery or grain mill the interval is apt to be short with substances like ragweed pollen the exposure is intermittent and the onset is delayed

Cooke's postulates[2] to prove that a sub stance can cause allergic symptoms are (a) the substance must give a positive local reaction or must be able to cause clinical symptoms, (b) the patient must be known to have been exposed to this substance

Allergens can cause asthma by inhalation, ingestion or injection Some allergens can act in more than one way, e g, wheat flour can cause asthma by inhalation and dermatitis by contact Some allergens can cause more than one set of symptoms, e g, egg can give rise to asthma, rhinitis, atopic dermatitis (eczema), migraine, urticaria, and gastrointestinal allergy

The chief allergens in bronchial asthma and rhinitis are

A Inhalants
   1 Pollen of trees, grasses, weeds
   2 Spores of fungi (molds, smuts, yeasts)
   3 Animal hair, dander, feathers
   4 House dust
   5 Cereals flour of wheat, corn, rye, etc
   6 Seeds of cotton, kapok, flax, etc
   7 Miscellaneous orris root (cosmetics), pyrethrum (insecticides), karaya gum (wave sets), certain powdered drugs, insects, etc
   8 Occupational dusts, e g, farmer, miller, furrier, baker, upholsterer domestic

B Ingestants
   1 *Foods* egg, wheat, milk, fish, pork, etc
   2 Drugs, especially aspirin

C Injectants
   1 Overdose of extracts used in hypo sensitization, especially pollen
   2 Dr
   3 Se antitoxin

D Miscellaneous Mode of action not too clear
   1 Bacteria and their products
   2 Parasites, e g, ascaris and taenia
   3 Physical agents, e g, cold or heat

The *inhalants* are undoubtedly the main factors in true bronchial asthma and allergic rhinitis Pollen causes seasonal hay fever and approximately 40% of all untreated hay fever sufferers sooner or later develop bronchial asthma While pollen differs in different sec tions, symptoms are due chiefly to the light,

TABLE I

SEX AND AGE OF ONSET OF 459 CASES OF BRONCHIAL ASTHMA[1]

	Paroxysmal		Chronic	
Age at Onset	*Male*	*Female*	*Male*	*Female*
0–9	95	49	13	25
10–19	16	28	12	16
20–29	18	32	5	17
30–39	17	14	9	14
40–49	10	14	15	14
50–59	3	2	7	10
60–69	–	–	2	2
Totals	159	139	63	98

TABLE II

OCCUPATIONAL ASTHMA AND RHINITIS[1]

Occupation	*Chief Allergens*
Aquarium suppl es	Derris root Water flea (fish foods)
Bakers	Wheat corn rye buckwheat, spices
Barber (and beautician)	Orris root henna dyes Karaya (Indian) gum tragacanth flaxseed quince seed hair sheepwool wool grease oil of citrus group essential oils
Bedding	(1) Feathers chicken duck goose swan pigeon turkey
	(2) Animal hair horse, rabbit goat cow hog cat sheep
	(3) Cottonseed kapok silk floss flaxseed
	(4) Straw corn husks wood shavings
Brushes	Animal hair cow hog horse goat sheep
Butchers	Hair cow sheep hog rabbit
	Insecticides preservatives
	Boxwood (sawdust) on floor
	Physical allergy (cold refrigerators)
Canners	Peas and beans infested with Indian meal moth
Clothing	Dyes
	Hair horse goat cattle cat dog rabbit camel sheepwool
Exterminators	Pyrethrum orris root chemicals (D D T)
Farmer	Vegetables (tomato workers Cladosporium) cereals etc
	Livestock and cats dogs rabb ts etc
	Poultry
	Corncockle
	Chicken coop mites molds smuts feed (Kamala)
	Pollen molds corndust (smut)
Florist	See Horticulturist
Flowers (artificial)	Feathers chicken duck goose swan turkey
	Silk
	Dyes
Flour mill workers	Grain smut and rust
	Wheat rye corn buckwheat
	Molds mites pollen
Furn ture	See Bedding
Furriers	Dyes
	Insecticides sawdust (boxwood) furs
	Fumes from cleaning fluids e g naphtha
	Im tation furs cat dog rabb t goat cow
Gloves	Hair rabbit horse sheep goat cat
Grain elevator operator	See Flour M ll Workers
Grocer	Coffee dust
	Flour dust
	Spices
	Boxwood (sawdust) on floor
Hat maker	Fabrics cotton wool, silk furs
	Feathers duck goose ostrich chicken pigeon
	Hairs horse goat, rabbit, sheep
	Bleaching agents banana oil oxalic acid dyes
Horticulturist (florist)	Flowers of all kinds Holland bulbs wormwood
	Hay straw grass mats pyrethrum
	Molds and fungi
	May and Caddis flies other insects
Housewife	House dust, feathers orris root pets pyrethrum (insecticide) D D T
Insulators	Animal hair goat rabbit hog
	Flax and straw
Jewelers	Boxwood (sawdust)
	Cuttlefish bone
	Orange stick
Laboratory worker	Hair guinea pig rabbit dog cat horse mouse sheep

TABLE II—Continued

Occupation	Chief Allergens		
Metal polishers	Rouge, resin, bichromate, oxalic acid, turpentine		
Painters	Linseed oil, dyes, lead		
Pharmacist	Acetyl sal acid	*Ipecac*	Poke root
	Arsphenamine	Lycopodium	Pyramidon
	Caroid	*Methyl salicylate*	Quinine
	Cocaine	Peptone	Rhubarb
	Codeine	Podophyllin	*Urease*
	Dichloramine-T		
Poultry	Feathers chicken duck, goose, turkey		
	Chicken feed linseed, castor bean soybean		
	Mites, smuts and rusts, kamala powder		
Printers	Acacia (offset spray), dyes, glue		
Rag sorters	Wool cotton silk, linen		
	Dust		
	Insects		
Refrigeration	Sulphur dioxide		
Rugs	Animal hair cat, rabbit, cow, sheep, wool, camel, goat		
	Lead		
	Dyes		
Shoe	*See Glove*		
Tobacconists	Tobacco (?)		
	Perfumes		
	Flavorings		
	Gum Tragacanth		
Tomato workers	Cladosporium (mold)		
Toys	Animal hair cat rabbit cow sheep, goat dog horse		
	Lead		
	Dyes		
	Glue		
Warehouse workers	Coffee		
	Dust		
	Cocoa		
	Flour smuts and rusts molds		
	Insects		
Wig makers	*Animal hair goat, horse sheep*		
	Also see Barber		

buoyant, wind-carried pollen of weeds, grasses and trees Pollen of flowers is carried by insects and is of little consequence Symptoms of hay fever are usually directly proportional to the amount of pollen in the air, but pollen *asthmatics frequently suffer during a thunder* storm or on other damp days when the pollen *count is low*

The importance of spores of fungi is becoming increasingly recognized The allergenic fraction of molds lies in the spores, extracts of mycelia being unimportant Clinically they resemble pollen in many respects especially in that symptoms are directly proportional to the mold spore count Alternaria and hormodendrum are the most important molds in some sections, but penicillium, aspergilli and other molds predominate in other parts of the world Grain smuts are important in asthmatic patients from the farm or flour mill When the mold count is high, excessive consumption of yeast (e g, drinking beer) may precipitate an attack of asthma whereas *such ingestion might have no such effect at* other times

House dust is one of the main causes of asthma It is a gray powder which exudes from aging bedding and soft furniture, but its exact nature is unknown There is some disagreement as to whether it does or does not contain a specific allergen, but it has been proven allergenic by skin and transfer tests.

by constitutional reactions from overdosage by anaphylaxis experiments in animals and especially by relief of symptoms by avoidance and by recurrence of asthma or rhinitis on re-exposure The dried decomposed bodies of insects and fungi may possibly be parts of the allergenic fraction of house dust

Animal danders especially from horses cats and dogs frequently cause asthma and rhinitis with brilliant results by avoidance supplemented in some cases by hyposensitization Those allergic to horse dander must be given tetanus and diphtheria toxoid as horse serum containing antitoxin may well cause anaphylactic shock and even death Such individuals should carry cards which warn against the use of antitoxins

The other inhalants are less important but as a group they cause symptoms in many patients Cottonseed is a potent allergen found especially in mattresses and in impure cottonseed oil Kapok should be avoided by all allergic individuals Orris root is becoming of less importance because manufacturers of face powders now usually omit it but it is still found in perfumes and gin

Farm dusts are mixtures of cereals molds rusts smuts insects and other substances Excellent skin test reactions are often found in patients from farms with good results on avoidance plus hyposensitization

Foods can also cause bronchial asthma and other allergic conditions especially in children Since ancient times it has been known that certain foods cause peculiar symptoms in certain individuals—"What is one man's meat is another man's poison" Eggs wheat milk and corn are probably the most important in this respect although other foods can cause attacks Antigenicity is lessened by heating therefore less sensitive patients can eat moderate amounts of cooked foods to which they are allergic If a person is allergic to a certain food he is apt to be allergic to other members of that food's genetic family e g the legumes

Drugs are rather infrequent causes of asthma but if a patient states that aspirin brings on an attack the wise physician will give strict orders to avoid aspirin and all aspirin containing drugs Terrific attacks of asthma and even death have resulted from carelessness in this respect Drug sensitive individuals should be given wallet sized cards on which the particular drug is named

Overdosage of extracts during hyposensitization may cause asthma rhinitis urticaria and shock its occurrence is greatly diminished by care during treatment

The role of bacteria is still hotly debated Some believe that they act as primary allergens Others deny this while conceding the great importance of bacterial infection in asthma and the good results sometimes obtained by the use of bacterial vaccines

Incidence of Asthma Asthma occurs in all races and all over the world in approximately 0 5% of the population There are about 500 000 to 1 000 000 cases in the United States but statistics are not too reliable as the condition need not be reported The mortality is low but the morbidity is high There is a slight predominance in males Asthma occurs at all ages but is especially important and frequent in the first decade of life these periods also offer the best prognosis if allergy management is promptly begun

Environment is very important especially as regards exposure to large amounts of house and occupational dusts pollens molds, and animals Social status climate altitude and seasonal variations probably act by lessening or increasing exposure to allergens but they may also influence respiratory infections

To aid in discovering the cause of asthma a chart on its relationship to occupation follows This is only a suggestive guide

PATHOLOGY OF BRONCHIAL ASTHMA

Pathological Physiology During attacks of asthma there is a reduction in *vital capacity* due chiefly to a marked increase of "dead space" (residual air) Vital capacity increases as improvement occurs In mild attacks the vital capacity may be only slightly reduced but even in such cases the patient cannot undergo as much and as prolonged exertion as

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	Insects		
Wig makers	Animal hair goat horse, sheep		
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[illegible]

zation may cause asthma rhinitis [illegible] shock its occurrence is greatly [illegible] care during treatment

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Environment is very [illegible] as regards exposure to [illegible] and occupational dusts [illegible] animals Social status [illegible] seasonal variat ons prob[illegible] or increasing exposure [illegible] may also influence resp[illegible]

To aid in discover[illegible] a chart on its relat[illegible] lows This is only a [illegible]

he can when he is entirely free from asthma A far more marked reduction occurs in the timed vital capacity, the first second measurement often being 30 to 40% of the total, as opposed to the normal of at least 75% Similarly the maximum breathing capacity, which is again a measurement of the ability to breathe rapidly, is markedly reduced The air velocity index

$$\frac{\text{The per cent of predicted maximum breathing capacity}}{\text{The per cent of predicted vital capacity}}$$

is markedly reduced in asthma and emphysema, and is an extremely accurate measurement of the degree of impairment

Another important factor is that the cartilaginous rings in the trachea are like horseshoes, open posteriorly, and aid in keeping the tube open During normal expiration air escapes more or less passively and without effort even though the anteroposterior diameter is diminished during this phase In asthma this collapse increases the dyspnea already present, and is probably the reason why expiration tends to be prolonged and more difficult than inspiration

Pathogenesis The partial obstruction which causes dyspnea and wheezing is chiefly due to edema of the walls with edematous fluid in the lumina of the lower respiratory tract Some of this watery material is exhaled and often leaves thick tenacious sputum and mucous plugs This material still further decreases the amount of available oxygen and adds to the severity of the asthma, this edema is easily demonstrated at bronchoscopy The plugs are frequently coughed up and seen grossly In addition mucous glands tend to secrete an excessive amount in asthma thereby increasing the symptoms

From ancient times most men recognized the spasmodic nature of asthma and many thought that this was due to a spasm of the bronchial tubes The theory of bronchospasm has lost many of its earlier advocates but spasm may play a part Alexander[3] says "In the earlier stages of the disease, edema and bronchial constriction are probably the most important factors since the mucous glands are small and the production of mucus scant In long standing asthma, increased, thick tenacious mucus is probably the most important factor in bronchial obstruction "

In chronic asthmatics, as Huber and Koessler[4] showed hypertrophy of the bronchial muscles may also occur and may add to the obstruction although it cannot be the whole cause

Some workers believe that histamine or a histamine like substance is elaborated during attacks of asthma by interaction of allergen and antibody in or at the sensitized bronchial cells Despite a large number of experiments this theory has not been proven and there is much evidence against it For example the so called antihistamine drugs like Benadryl® and Pyribenzamine® have been singularly ineffective in all but the mildest cases of asthma The role of serotonin also awaits clarification

Pathology Deaths during attacks are uncommon but do occur, especially in older patients with chronic asthma Injections of morphine not infrequently precede exitus and this drug should never be used during attacks of bronchial asthma because it lessens the cough reflex and slows respiration thereby increasing anoxia Atropine tends to dry secretions and therefore can be harmful in asthma Iodides on the other hand loosen the sputum and that is why they are effective

TABLE III

CAUSES OF DEATH IN BRONCHIAL ASTHMA[1]

1	Asthma main or sole cause	21 cases*
2	Asthma a contributory factor	16 cases
3	Other causes (Asthma not a factor)	11 cases

* Morphine known to have been injected prior to death in 6 of these patients

Complications are frequent e g chronic infectious bronchitis or pneumonitis bronchiectasis sinusitis and nasal polyposis Less frequent are spontaneous pneumothorax and subcutaneous and mediastinal emphysema as well as fractured ribs The heart is rarely affected in allergic asthma although heart disease and asthma may coexist Table III summarizes the causes of death in 459 cases of asthma over a 20 year period

Autopsies in bronchial asthma usually reveal

1 Emphysema with pressure of enlarged lungs against the chest wall with overlapping of the heart

2 Localized areas of atelectasis

3 Thickening of the bronchial muscles in chronic cases

4 Increased secretion in the walls and lumina with many mucous plugs

5 Widespread eosinophilia in the walls the lumina and in the plugs

6 Thickening and hyalinization of the basement membrane of the bronchi

7 In most cases there are also one or more complications e g chronic infectious bronchitis or pneumonitis bronchiectasis sinusitis and nasal polyposis

In paroxysmal asthma these changes may be reversible but they are more or less irreversible in chronic asthma with emphysema The many autopsy reports in asthma are summarized by Unger[5] together with details of five cases in which death occurred in patients with uncomplicated bronchial asthma

SYMPTOMATOLOGY

Dyspnea orthopnea wheezing and cough are the main symptoms in bronchial asthma These may occur in attacks (*paroxysmal asthma*) with reversible changes and with a good prognosis or symptoms may be constant (*chronic asthma*) with pathological changes which are usually irreversible

In patients who have attacks of asthma symptoms are absent in the free intervals In many who think they are entirely symptom free between attacks however questioning may reveal a little dyspnea on such exertion as would not affect normal people and a little wheezing may be heard with the stethoscope Pulmonary function tests also may reveal significant abnormalities especially in the timed vital capacity

In *paroxysmal asthma* symptoms may be mild to severe In the mild group there is a little dyspnea especially on exertion a little cough some wheezing (best heard with a stethoscope) and perhaps some expectoration Fever is rare in adults common in infants and young children A little ephedrine or epinephrine usually suffices and the patient is able to continue with his usual activities

In the moderate cases the symptoms are more severe The patient may be in bed because of orthopnea wheezing and dyspnea A little exertion is possible The attack may last longer but usually responds to one or more injections of epinephrine and/or aminophylline

In the more severe paroxysmal cases symptoms may start slowly or suddenly and the patient becomes bed ridden and gasps for breath cyanosis and tachycardia are common. Expiration is usually prolonged and wheezing often loud Such attacks may last from a few hours to about four days but the patient almost always makes a complete or almost complete recovery and is well until the next spell Steroid therapy is often necessary during the acute attack

In *chronic asthma* symptoms also range from mild to severe Many patients wheeze and cough every day but manage to keep on with their work provided the work demands little exertion Some patients are more or less incapacitated and are termed "intractable asthmatics

Status asthmaticus is the most severe stage of chronic asthma Suffering is severe with loss of weight, strength and morale An infectious complication is often present e g bronchitis or pneumonitis as evidenced by clusters of crepitant rales low fever leukocytosis and increased sedimentation rate In some of these "infectious asthmas" the chest x ray may show mottling Rapid pulse cyanosis excessive perspiration and marked dyspnea and orthopnea are common Even eating is an exertion which increases the symptoms Status asthmaticus with proper treatment can almost always be overcome especially since the introduction of the steroids Death may occur but is uncommon unless morphine is given

Asthma in children is usually of the paroxysmal type and often associated with fever

Chronic asthma is more frequent in older life and is usually present when the onset occurs after the age of 40 to 50 Asthma in older age groups is often complicated by other causes of dypsnea

Eosinophilia in the blood and sputum is common and the sputum frequently contains Curschmann s spirals and Charcot Leyden crystals Various biochemical studies have shown no significant abnormalities of blood calcium phosphorus potassium sodium and magnesium levels Blood sugar level is usually normal or low there is a tendency to *gastric hypo acidity*

DIAGNOSIS

The diagnosis involves *three considerations* Is bronchial asthma present? What complications if any exist? What causes the attacks?

I DIRECT DIAGNOSIS

The *diagnosis of bronchial asthma is usually* relatively easy and is based on

A *History* of attacks of wheezing dyspnea orthopnea and cough In paroxysmal asthma the patient states that he is normal between spells In chronic asthma symptoms are more or less continuous often with exacerbations

B *Examination wheezing and prolonged* expiration are usually present over all parts of both lungs The heart is often small and heart tones are frequently best heard in the epigastrium (since the heart is often overlapped by emphysematous lungs) Fluoroscopy usually reveals an elongated or normal sized heart and a low diaphragm with lessened excursion In chronic asthma increased intercostal spaces and hilar and bronchial markings are common

C *Eosinophilia* is usually present in the blood *(up to about 20%)* and *often much* higher in the sputum (up to 100%) A Wright or similar stain should be made routinely with sputum as well as the Ziehl Neelsen stain for tubercle bacilli A high eosinophil count in sputum *is also of great diagnostic importance* in allergic bronchitis a condition which may precede true bronchial asthma but in which wheezing and dyspnea are absent Nasal allergy is often associated with allergic asthma and nasal smears usually *show eosinophiles in* such cases

D Relief from epinephrine aminophylline and the corticosteroids in certain cardiac con*ditions these* drugs can also lessen dyspnea

E Positive skin tests clinically corroborated (see below)

F Allergy in the family or other allergic conditions in the patient

It must be emphasized that any of these findings can occur in non allergic conditions *The more of the above findings however the* more certain is the diagnosis of bronchial asthma

II COMPLICATIONS

A Emphysema is probably always present *with chronic asthma* The *alveoli* enlarge because there is incomplete blocking of the lower respiratory tract Permanent deformities of the chest frequently follow these varying according to the age of onset and the *severity of symptoms The sternum may be* indented in young children older children tend to develop pigeon breast and adults the barrel type Breath sounds are distant When the enlarged lungs overlap the heart heart tones are frequently best heard in the *epigastrium* Except in children emphysema rarely disappears and may progress to the point of complete disability The presence of emphysema in young children if it is to be successfully reversed demands immediate and proper allergy management

B Infectious complications are frequent especially in chronic asthma These include bronchitis and pneumonitis which are often readily controlled by antibiotic therapy When an asthmatic patient has fever leucocytosis *increased sedimentation* rate and clusters of crepitant rales in addition to wheezing he almost certainly has a complicating infection in the lungs and should receive *antibiotics*

Whether or not the bacteria and their products act as antigens to produce asthma in the presence of infection antibiotics often give dramatic relief in such patients

C Bronchiectasis may also be present although asthma is not necessarily the cause It should be suspected if the morning sputum is profuse and fetid if bubbling rales are heard or if hemoptysis occurs The diagnosis can only be clinically confirmed by bronchograms The dilatations may be tubular or saccular and are especially frequent in the lower lobes

The exact relationship between bronchiectasis and bronchial asthma is not clear The two can occur together possibly independently Watson and Kibler[6] from Arizona stated that in 90% of all of their cases of bronchiectasis a diagnosis of allergy was made from the history positive skin tests associated allergic conditions and by the presence of at least 10% of eosinophils in the nasal or bronchial secretions They believed that the process began with a basal bronchitis followed by atelectasis and then dilatation of bronchi In our experience this high percentage does not occur, we agree with Bullen[7] who found bronchiectasis in only 7 75% of his asthmatic patients

Bronchiectasis is a fairly common condition dyspnea is not important wheezing occurs in many cases Not all are allergic however as anything which partially obstructs the respiratory tract can cause wheezing We agree with Mallory[8] who stated that bronchial asthma rarely if ever causes bronchiectasis when they occur together coincidence is more likely Furthermore in the great majority of bronchiectatic lungs there is no evidence of narrowing of the bronchial tree proximal to the areas of dilatation Mallory believes that only the assumption of a primary infectious bronchitis with secondary atelectasis with or without pneumonitis can explain the occurrence of bronchiectasis Congenital malformations and bronchostenosis are unimportant causes

D Atelectasis is undoubtedly very common in bronchial asthma but most areas are small It follows complete obstruction of a bronchiole If a large bronchus is obstructed "massive atelectasis or "massive collapse" occurs a whole lobe may become airless and in asthma this is usually due to a mucous plug with relief on expectoration of the plug or after removal through a bronchoscope In such a massive obstruction the breath sounds are usually absent on the affected side and the mediastinum may be pulled toward that side

E Spontaneous pneumothorax is not infrequent An emphysematous vesicle or a lobule may rupture from over distension during an attack of asthma Pain dyspnea orthopnea and cyanosis may occur suddenly or slowly depending on the size of the opening Tympany and absent breath sounds occur on the affected side and the heart is pushed toward the opposite side Recovery is usual but deaths have resulted

F Subcutaneous emphysema is less frequent but more dangerous It may occur with spontaneous pneumothorax and is due to the rupture of one or more air sacs at the hilus or periphery the air may migrate into the mediastinum and neck and may reach the face Crepitation on pressure is diagnostic proper reading of x ray films is also revealing

G Attacks of asthma may be so severe that one or more ribs are fractured Localized pain suddenly occurs especially on deep breathing and localized tenderness and swelling are usually present There is seldom any displacement and healing is rapid Adhesive taping is advised

H Nasal polyposis is very common in chronic asthma The nasal mucosa becomes edematous If the condition persists the weight of the fluid forces the mucosa to hang down more and more until grape like pale tissue can be seen The polyps may be small or so large as to block the nostrils and even to reach the exterior nares In all cases there is coincident polyposis of one or more of the accessory nasal sinuses removal of nasal polyps is frequently followed by the later appearance of other polyps which have emerged from the sinuses Nasal polyps are almost certainly the result of allergy and if they are not too large they may disappear when proper allergy measures are carried out Steroids

Chronic asthma is more frequent in older life and is usually present when the onset occurs after the age of 40 to 50. Asthma in older age groups is often complicated by other causes of dyspnea.

Eosinophilia in the blood and sputum is common and the sputum frequently contains Curschmann's spirals and Charcot-Leyden crystals. Various biochemical studies have shown no significant abnormalities of blood calcium, phosphorus, potassium, sodium and magnesium levels. Blood sugar level is usually normal or low; there is a *tendency to* gastric hypo-acidity.

DIAGNOSIS

The diagnosis involves three considerations:
Is bronchial asthma present?
What complications, if any, exist?
What causes the attacks?

I. DIRECT DIAGNOSIS

The diagnosis of bronchial asthma is usually relatively easy and is based on:

A. *History* of attacks of wheezing, dyspnea, orthopnea and cough. In paroxysmal asthma the patient states that he is normal between spells. In chronic asthma symptoms are more or less continuous, often with exacerbations.

B. *Examination*: wheezing and prolonged expiration are usually present over all parts of both lungs. The heart is often small, and heart tones are frequently best heard in the epigastrium (since the heart is often overlapped by emphysematous lungs). Fluoroscopy usually reveals an elongated or normal sized heart and a low diaphragm with lessened excursion. In chronic asthma increased intercostal spaces and hilar and bronchial markings are common.

C. *Eosinophilia* is usually present in the blood (up to about 20%), and often much higher in the sputum (up to 100%). A Wright or similar stain should be made routinely with sputum as well as the Ziehl-Neelsen stain for tubercle bacilli. A high eosinophil count in sputum is also of great diagnostic importance in "allergic bronchitis," a condition which may precede true bronchial asthma, but in which wheezing and dyspnea are absent. Nasal allergy is often associated with allergic asthma, and nasal smears usually show eosinophiles in such cases.

D. Relief from epinephrine, aminophylline, and the corticosteroids; in certain cardiac conditions these drugs can also lessen dyspnea.

E. Positive skin tests, clinically corroborated (see below).

F. Allergy in the family or other allergic conditions in the patient.

It must be emphasized that any of these findings can occur in non-allergic conditions. The more of the above findings, however, the more certain is the diagnosis of bronchial asthma.

II. COMPLICATIONS

A. Emphysema is probably always present with chronic asthma. The alveoli enlarge because there is incomplete blocking of the lower respiratory tract. Permanent deformities of the chest frequently follow, these varying according to the age of onset and the severity of symptoms. The sternum may be indented in young children, older children tend to develop pigeon breast, and adults the barrel type. Breath sounds are distant. When the enlarged lungs overlap the heart, heart tones are frequently best heard in the epigastrium. Except in children emphysema *rarely* disappears and may progress to the point of complete disability. The presence of emphysema in young children, if it is to be successfully reversed, demands immediate and proper allergy management.

B. Infectious complications are *frequent* especially in chronic asthma. *These include* bronchitis and pneumonitis which are often readily controlled by antibiotic therapy. *When* an asthmatic patient has fever, *leucocytosis*, increased sedimentation rate and *clusters of* crepitant rales in addition *to wheezing*, he almost certainly has a *complicating infection* in the lungs, and should receive antibiotics

the attacks? What about idiosyncrasy to foods or drugs? Are there periods of freedom and if so why? The patient s home and occupational exposures are carefully brought out as possible causes of attacks The history of previous or family allergies is taken and the information regarding past illnesses, habits etc are obtained A good history may be diagnostic e g asthma after exposure to horses or flour or after eating eggs

B Further information may be obtained by having the patient avoid suspected allergens e g a dog or wheat or feather pillows If symptoms clear on avoidance they may return when exposure is tried Such clinical tests are even more corroborative than are positive skin tests

C Further information may be obtained from correlation of the patient s symptoms with the atmospheric pollen or mold counts If asthma and/or hay fever occur each August and September when ragweed pollen is in the air the cause of the attacks is usually self evident In almost all of these cases positive skin tests are obtained with ragweed pollen extracts Molds too may cause seasonal symptoms as with pollen the symptoms generally reaching their peak in July–September (in the North Central States)

D Skin tests It is necessary to test for all substances which might conceivably be important If complete tests are not carried out important causes may be missed One cannot rely on the history alone to determine what tests to do e g one allergic to cottonseed *rarely realizes this fact until informed by the* skin test The practice of doing 20 to 30 tests on a child and informing the parent that skin tests have been carried out is reprehensible it is of no more value than is the incomplete physical examination Each substance should be tested individually group tests may fail because of dilution

The following is part of a recent article [16]

Skin tests are usually carried out either by the scratch or intracutaneous methods or by both Information can also be obtained by using the passive transfer technique by conjunctival and nasal tests and by clinical experiments

Skin tests offer us a valuable short cut and often reveal causes which cannot be found even after a searching history and clinical trials All positive skin tests however must be corroborated clinically

A Scratch (Cutaneous) tests were first carried out by Blackley of England in 1873 [17] with positive reactions to grass pollen in those who had hay fever and/or asthma during grass pollinating seasons Previously however Hyde Salter[18] had noted positive reactions in his own skin from the scratch of a cat s paw In this century rapid progress has been made in skin testing In 1912 Schloss[19] found positive reactions in a child who was allergic to egg almond and oat Walker[20] in 1916 reported 400 patients with asthma and divided them into two groups sensitive with positive skin tests and nonsensitive in whom the scratch tests were negative

Scratch tests have proved extremely valuable all through these many years They are not perfect but they are widely used are safe and can be easily done The materials are either liquids which are rubbed into a scratch or powders which are dissolved with N/10 sodium hydroxide and then rubbed into the scratch

B The Intracutaneous (Intradermal) Method was started and popularized by Cooke and his associates[21] in 1915 Their students have continued to use this intradermal method those who followed Schloss and Walker have used the scratch technique For many years controversy has existed between the exponents of these two procedures and even to this day many allergists use only one or the other Fortunately most of us have learned the good points of each method and we use both techniques

Intracutaneous tests are done with sterilized solutions needles and syringes Larger reactions are usually obtained by these injections into the skin and frequently we find a positive intradermal test after a scratch test for the same allergen has been negative

Systemic reactions and even death have occasionally *occurred when intradermal tests have* been made without a previous negative scratch test Swineford [20] for example reported death in one patient and anaphylactic shock in another both received intradermal tests with a mustard extract and neither patient had previously been tested for mustard by the scratch method Swineford concluded his article by stating "Every intradermal test should be preceded by the less sensitive scratch test "

We believe that scratch tests should be made first If that technique gives us enough information intradermal testing is not necessary For example if hay fever and asthma occur each year when the grasses are pollinating and if scratch tests are strongly positive for the various grass pollen extracts intradermal testing with these extracts is not necessary and in fact could cause systemic reactions If however scratch testing

are *remarkably successful* in reducing their size at least temporarily Nasal smears in such cases almost always reveal a high per centage of eosinophiles In some patients *polyps cause asthma* by a trigger mechanism by pressure with relief on removal of the polyps

I The heart is rarely affected by bronchial asthma Numerous studies have been made on the effects of chronic asthma on the cardiac structures—clinical electrocardiographic and at autopsy From these we can conclude that *cardiac decompensation rarely follows* bron chial asthma unless the patient also has an *associated cardiorenal disease* e g hyperten sion rheumatic syphilitic or congenital heart disease *Most asthmatic patients* have as good or better hearts as normal persons of equivalent ages

This optimistic attitude has been expressed by many *In 1839 Andral*[9] *said that asthma* "is a brevet of long life" Oliver Wendell *Holmes agreed that asthma* "is the slight ail ment that promoted longevity Bray[10] says that *Many asthmatics pant on to a good old age* Alexander[11] believes that during an at tack the quantity of blood which enters the right heart is diminished thereby actually sparing the heart These opinions are con firmed by Criep[12] and others

Several articles have appeared which chal lenge this optimistic point of view Dublin and Marks[13] say that the mortality in asth matics is about two and one third times the normal but their figures are taken from death certificates which are not always accurate In some of their cases of "death from asthma organic heart disease (cardiac asthma) was probably responsible for death rather than the bronchial asthma itself

From the electrocardiographic point of view however chronic asthma does tend to change the axis to the right as shown by Unger[14] Colton and Ziskin[15] and others Tracings often show right axis deviation Yet even in such cases there seems *to be no tendency* to decompensation unless as stated there is an associated cardiorenal disease

J Cor pulmonale is extremely rare in un complicated bronchial asthma We have never seen such an outcome unless the patient had some other pulmonary condition e g severe bronchiectasis silicosis cystic lungs wide spread fibrosis or severe kyphoscoliosis

Since asthma occurs at any age it can of course be associated with any other condition Tuberculosis is rather rare in asthma though the two can occur coincidentally In addi tion chronic pulmonary tuberculosis can cause narrowing of the respiratory tract with con sequent wheezing which is usually unilateral and more or less constant Diabetes mellitus is not infrequent in asthmatics Heart disease is more commonly associated especially hy pertension coronary disease and valve in volvements Carcinoma of the lung may de velop in patients with true asthma More fre quently wheezing occurs in certain patients who have carcinoma of the bronchi in such cases the diagnosis of bronchial asthma may be made but wrongly

III CAUSE OF ATTACKS (SPECIFIC DIAGNOSIS)

The specific cause of the attacks may be readily apparent or may require all of the diagnostic methods at our disposal The methods by which the offending allergens can be ascertained are as follows

A Histories should be taken very carefully The patient should be encouraged to talk without interruption and the detective nature of the inquiry explained The circumstances of all of the attacks should be drawn out yet leading questions are to be avoided if pos sible The season the time of attacks the exposures etc are to be noted on the history sheet It is especially important to classify the symptoms as paroxysmal or chronic as this helps in determining the prognosis and treat ment Almost every true asthmatic wheezes coughs and has dyspnea and *orthopnea* If there is no orthopnea the diagnosis of bronchial asthma at *once becomes uncertain* (except in infants) Fever is rare in uncomplicated asthma (except in children) Expectoration is usually difficult in asthma especially when the attack begins whereas it is usually easy and profuse in bronchiectasis

When the patient has finished his story we ask specific questions e g what brings on

in two groups i e, diseases of the upper or lower respiratory tract

I *Diseases of the upper respiratory tract* are frequently associated with stridorous breathing (inspiratory wheeze plus dyspnea) In bronchial asthma the expiratory wheeze is almost always more evident than the inspiratory Among obstructive lesions may be mentioned

A Severe nasal deformities with resultant snore

B Large tonsils and adenoids occasionally

C Laryngismus stridulus in infancy (some believe this may be a first symptom of asthma)

D Localized tumors e g, carcinoma of the trachea

E Laryngeal diphtheria

F Paralysis of the vocal cords from any cause

G Lesions which press on the larynx trachea or primary bronchus e g enlarged thymus substernal goiter retropharyngeal abscess aneurisms, enlarged lymph nodes (Hodgkin's disease leukemia tuberculosis etc) and various types of tumors, especially carcinoma

H Foreign bodies as emphasized by Chevalier Jackson and his "All is not asthma that wheezes"[20] In a recent case [7] the typical bilateral asthma in a little girl persisted until atelectasis of the right middle lobe occurred and then a peanut was aspirated via bronchoscopy

In all of the above lesions the correct diagnosis should not be too difficult A thorough history and examination including x ray and laboratory tests should be diagnostic There is usually no history of allergy in the patient or in his family wheezing if present is usually chiefly inspiratory eosinophilia is uncommon but can occur In a recent patient with carcinoma of the tracheal carina there was 100% eosinophilia in one sputum specimen Wheezing was chiefly inspiratory and openings to both main bronchi were almost completely closed by squamous cell carcinoma as shown by biopsy Eosinophilia can also occur in other non allergic conditions e g Hodgkin's disease and leukemia

The following cases represent some of our recent problems[23]

Case I B A age fifteen This girl was referred July 17 1950 because of asthma" She had bronchitis at nine with severe "cold" and cough For the past three months "bronchitis had recurred again and again as shown by dyspnea orthopnea cough rattling in the chest and wheezing Ten days ago her "asthma" suddenly became violent and she was in a hospital for two days with relief after oxygen and intravenous fluids Adrenalin was not given There were no nasal symptoms but the girl had lost 15 pounds in one month

She was worse at night and after exertion and received little benefit from Pyribenzamine® and ephedrine Her past history revealed pneumonia scarlet fever mumps and chicken pox and removal of tonsils and adenoids The family history was negative for allergy The urine Kahn test blood and sputum were negative with 3 per cent eosinophils in the blood and none in the sputum

Examination revealed a well nourished white girl with no dyspnea at that time Resonance was good over both lungs but breath sounds were almost entirely absent on the right side especially the lower two-thirds The other lung was normal and wheezing was absent The heart was not displaced and the examination was otherwise negative On fluoroscopy the excursion on the right side was diminished and x ray films were unremarkable We did notice that inspiratory sounds on the right side were a little rougher than those on expiration

We therefore concluded that her dyspnea and wheezing and the almost complete absence of breath sounds on the right side must be due to an obstruction of the right primary bronchus Because she was only fifteen the diagnosis of a bronchial adenoma suggested itself

Bronchoscopic examination (Dr Jerome Head) revealed a "normal larynx and trachea About half way to the carina a tumor mass was found projecting from the right lateral wall of the trachea partially obstructing the lumen Pieces were secured for microscopic study and in the process there was free bleeding " One week later more tumor tissue was removed and on the third week the rest was removed through the bronchoscope or was coughed up one chunk was as large as the end of her thumb A week later re examination showed that the tumor was gone though the remainder of the pedicle was seen to come from an elongated patch 5 x 10 mm The carina was markedly widened and looked inflamed

Tissue examination established the fact that the tumor was a leiomyoma rather than an adenoma Her so-called "asthma has disappeared Skin tests of course were not carried out as there was no evidence of allergy The patient has been asymptomatic for the past seven years

Case 2 Mrs J C age forty-one entered Wesley Memorial Hospital because of "asthma"

does not yield sufficient information, testing by *the intracutaneous method must follow*, and will frequently be successful even when the scratch tests were negative To solve some allergic problems, one frequently has to use every available method, just as one does who tries to solve a *murder mystery The allergist is a detective*

C The Passive Transfer method was invented in 1921 and named after its authors, Prausnitz and Kustner[23] "The substance responsible for the immediate positive skin reaction in hay fever and asthma is *present in the patient's blood and can* be transferred to and fixed in a normal skin by an intracutaneous injection of the patient's serum This antibody, designated as atopic reagin by Coca and Grove,[24] is specific for each atopen" (Walzer) [25]

This indirect method of testing by no means takes the place of the usual scratch and intracutaneous techniques It need be used only occasionally, when direct testing is impractical, especially when the patient's skin is covered with eczema or cannot be used because of severe dermographia

D *The Conjunctival method is occasionally used* to test pollens, fungi, or animal danders, but is only tried when both the scratch and intracutaneous techniques have proved negative

E The *nasal method can be tried with such materials as fungi or perfumes*

Value of Skin Tests in Allergy of the Respiratory Tract

Skin tests are indispensable in these allergic conditions Positive reactions are *usually obtained* when the history indicates allergy to a specific food or inhalant material, and when the test is positive the patient's suspicions are verified to the satisfaction of the patient and the physician *Some physicians seem content* with the patient's observation that egg, for example, causes his asthma Occasionally, in such a case, the skin test to egg extract proves negative both with the scratch and intradermal techniques, and then one looks for a different cause—the asthma may be due not to the egg but to bacon which has been in the same pan

No physician has time or inclination to ask regarding every possible cause for symptoms In one of our patients, for example, we were able to relieve asthma by removing a dental *adhesive used* to keep his upper plate in position *This adhesive* contained karaya gum The patient gave a four plus reaction to karaya gum extract which we had not previously suspected Cottonseed protein is a rather *frequent cause of severe asthma, yet the* cottonseed-sensitive patient does not suspect this unless he has had previous *skin tests Removal* of cottonseed and impure cottonseed oils usually brings almost immediate relief Some patients complain of hay fever, but *their seasons may not* be exactly synchronous with those of the usual pollens, in such cases skin tests frequently indicate that molds and smuts cause or aggravate symptoms, and the patient needs hyposensitiza

especially with food extracts, positive skin tests may occur, yet are unrelated to the cause of the symptoms

The positive skin test constitutes just another clue, but a valuable one It usually indicates a clinical allergy, but this allergy may be past, present or future The student of allergy soon learns *this fact*, and *he* also *learns that positive* skin tests in dermographic skin must be minimized

He also learns that skin tests are frequently lessened in size or absent in asthmatic patients who *are receiving such medication as ephedrine, epinephrine, or antihistaminic drugs* He therefore postpones skin testing in such cases until these drugs are presumably out of the system (three to seven days)

Steroids however, do not interfere with these tests and may be used to give the patient relief until the tests are completed This procedure is very important especially in severe asthmatic patients, *in such cases* the corticosteroids may be substituted for the other drugs which lessen skin test reactions

Nevertheless, despite some *shortcomings* skin

important approach to dis

results must be correctly interpreted They

successful in at least 75% of all cases of bronchial asthma

In doubtful cases of food allergy much useful information can frequently be obtained by elimination diets and feeding trials Food diaries are also helpful

DIFFERENTIAL DIAGNOSIS

The diagnosis of bronchial asthma *is usually* easy, but the condition must be differentiated *from* all *other* causes of dyspnea, wheezing, orthopnea and cough These can be placed

age After four weeks he signed a release and returned to his work as a printer We learned that he died some months later This was to be expected as the prognosis in this type of heart disease is unfavorable

TABLE IV

Bronchial Asthma	*Acute Cardiac Dyspnea (Cardiac Asthma)*
Paroxysmal dyspnea (*allergic*)	Paroxysmal dyspnea (*cardio-renal*)
History previous attacks	Attacks very few
Obstruction lower air passages	Pulmonary edema (failure left ventricle)
Onset in early life	Onset after 40 usually
Allergy in patient and family	Hypertension coronary disease aortic regurgitation, chronic nephritis
Eosinophilia blood and sputum	Absent
Wheezing prolonged expiration all over both lungs	Moist rales especially at bases some wheezing
Warm perspiration	Cold clammy skin
Condition usually good	Often in shock
Heart usually small	Heart dilated
Pulse good	Pulse often thready irregular
No fear of death	Fear of death
Epinephrine and aminophylline usually give relief morphine dangerous	Morphine best also digitalis and venesection epinephrin doubtful
Positive skin tests usually	Negative
Elimination of cause gives relief often complete	Rest in bed etc prolongs life
Circulation time normal	Circulation time prolonged

B Fibroid tuberculosis may also cause wheezing and some dyspnea but the wheezing is localized and apt to be more or less constant Epinephrine and aminophylline are usually ineffective Showers of crepitant rales are usually present and the correct diagnosis should be made by these findings plus the presence of fever tubercle bacilli in the sputum distinctive x-ray findings and the absence of allergic features Tuberculosis and true bronchial asthma can coexist

C Pneumoconiosis is a chronic condition which may be characterized by pulmonary fibrosis from inhalation of various kinds of irritants In such cases connective tissue is formed and tends to obliterate bronchial lumina Wheezing and dyspnea result and may gradually become so extreme as to cause complete incapacity The correct diagnosis is usually evident by the history of exposure the occasional wheeze the tendency to cor pulmonale and the absence of allergic involvement X-ray films especially in the nodular types are very helpful

Case 5 Mrs O C Negro age thirty five was admitted via ambulance wheezing and gasping for breath were severe She could not lie down and her ankles and legs were very edematous The heart was dilated and the liver was palpated 3 cm below the costal arch

She had been well until five years previous to admission She went to a clinic because of dyspnea on exertion and epigastric pains The findings at that time were not remarkable, but x-ray films showed an infiltrating process in both mid lung fields At that time she had some ankle edema after prolonged standing or walking One year ago she had had bronchopneumonia with gradual recovery but wheezing persisted

At the hospital on this admission urinalysis revealed 10 mg albumin per 100 cc There were 3 700 000 erythrocytes and 5,500 leucocytes including 1 per cent eosinophils Three sputa disclosed 45 90 and 23 per cent eosinophils, respectively with no acid fast bacilli on smears or cultures nor after injection into a guinea pig The total protein was 6 12 gm with 2 84 albumin and 3 28 globulin per 100 cc The nonprotein nitrogen calcium phosphorous and alkaline phosphatase were normal Repeated examinations of sputum and bronchial smears were negative for yeasts molds and other fungi and cultures showed some Diplococci pneumoniae and Staphylococcus aureus Bronchoscopy revealed edematous bronchial mucosa which bled easily but there was no evidence of obstruction Skin tests were negative for tuberculosis histoplasmosis coccidioidomycosis and brucellosis Stools were also normal An electrocardiogram showed findings consistent with early right heart strain

The x-ray films showed areas of increased density scattered throughout both lungs especially in the middle two-thirds Pulmonary fibrosis was suggested and one could see little change in the lungs between 1946 and 1951 The 1951 film showed that the heart had become much larger

Treatment on admission consisted chiefly of bed rest digitoxin Mercuhydrin* and some aminophylline The edema disappeared and the liver became smaller but the wheezing dyspnea and orthopnea persisted and several attacks of so-called "asthma" occurred from time to time

for about four months The wheezing and dyspnea became progressively worse, and vomiting and slight fever were also present She was known to have had a carcinoma of the uterus and vagina for the past six years, with apparent quiescence after inten... moderately ... nea, wheez... aminophylline gave some relief On standing in front of the patient, and without the use of a stethoscope, we noted that the wheezing was more marked on inspiration and that it really constituted a stridorous type of breathing This fact at once ruled out the diagnosis of bronchial asthma, in which, of course, wheezing and dyspnea are almost always more marked on expiration We abandoned the diagnosis of true allergic asthma despite the fact that successive examinations of the sputum showed that 2, 80 and 100 per cent of the cells were eosinophils

Our diagnosis was necessarily an obstructive lesion in the larynx or trachea Laryngoscopy was normal, but on bronchoscopy the carina was very broad and bulged into the bronchi, and was so swollen that only a narrow slit was visible at the entrance to the right main bronchus, and a small round opening on the left side The tissue was firm and red but did not bleed Two pieces were removed, with the diagnosis of squamous cell carcinoma We were unable to save her life

Case 3. Mrs D G, white, age eighty-one, was seen at Cook County Hospital, "Bronchial Asthma" was the admitting diagnosis, and some relief was obtained from aminophylline and epinephrine Her wheezing and dyspnea, however, were also more marked on inspiration, and stridor could be clearly heard without a stethoscope Percussion showed marked dullness in the right upper chest, and the ... there ... ... a ... nosis of a large substernal goiter seemed logical Surgery was advised but refused She went home with her dyspnea and wheezing and returned a year later, with death from terminal bronchopneumonia Autopsy revealed a huge colloid goiter which had grown around the trachea and which compressed the right primary bronchus It could probably have been completely removed

II *Non allergic diseases of the lower respiratory tract* may also simulate bronchial asthma In these, dyspnea is more prominent than wheezing, nevertheless they may cause confusion especially if the patient also has bronchial asthma Any cardiac or pulmonary disease can also lead to dyspnea as can anemias and some functional disorders

A "Cardiac asthma" is a term given to a paroxysmal condition due to sudden failure of the left ventricle This is purely a cardiac condition but is often confused with bronchial asthma because both cause paroxysmal nocturnal dyspnea and are characterized by wheezing The similarity of names has caused more confusion than the similarity of symptoms

The main features of "cardiac asthma" are the older age, presence of cardiac disease involving the left ventricle (hypertension, coronary disease, luetic aortic regurgitation, or nephritis) and especially the finding of many moist rales at both lung bases The wheezing is coarse and not at all like the fine musical high pitch characteristic of bronchial asthma

The differential diagnosis is emphasized because lives can be saved by giving epinephrine to the patient with bronchial asthma, and morphine to the individual with the much more serious "cardiac asthma" (see Table V) Aminophylline, of course is valuable in both, and can be used in case of doubt as to which is present

Case 4 Mr A G age seventy seven, was ad... venous injection of aminophylline This was his first attack, and there was no history of allergy in the patient or in his family This attack began five hours before admission, and there was no complaint of pain

Examination revealed a moderately nourished elderly, white male in very acute distress He was almost moribund and the so called "death rattle" was easily heard without a stethoscope Cyanosis and tachycardia were present There were watery rales all over both lungs His heart seemed dilated and his blood pressure was 150/90 An occasional wheeze was also heard, and the liver edge was not made out The lower extremities were not swollen

The diagnosis was at once changed to "acute cardiac dyspnea" (cardiac asthma, acute suffocative pulmonary edema) He was given one fourth grain morphine and 1/150 grain atropine, repeated in two hours Oxygen was given by inhalation and digitalis intramuscularly, and we assured the man that he would be much better very quickly In about ten minutes he was much better—he became quiet, there was less rattling and by evening his dyspnea was almost gone

We kept him quiet as long as we could, and electrocardiograms showed extensive cardiac dam-

fluoroscopy and chest x ray A history of having been in endemic areas e g the San Joaquin Valley (coccidiomicosis) or the Ohio or Missouri Valleys (histoplasmosis) is helpful and fungus skin tests are of value Finding the organisms in the sputum is diagnostic but this usually requires special culture media and well trained personnel

G Functional (sighing) dyspnea is not rare A few individuals take deep sighing breaths as they feel that they are not getting enough air If the deep breathing continues for some time tetany may result Cure is often easy the patient is shown how to breathe normally

H Carcinoma of the lung may lead to confusion in diagnosis if the tumor occurs in a large bronchus wheezing cough and dyspnea may be rather marked and mistakes in diagnosis common This constitutes a great tragedy because lobectomy or pneumonectomy may successfully be carried out if the diagnosis of carcinoma is made early enough The presence of localized wheezing of persistent cough especially in an older patient of hemoptysis and the absence of evidence of allergy should make one suspicious Examination by bronchoscopy and x ray may be diagnostic in the early stages when surgery is still feasible When the later findings of carcinoma ensue e g loss of weight and strength fever and severe hemoptysis surgical

TABLE V

Carcinoma Lung	*Bronchial Asthma*
1 Usually no allergy in patient or family	1 Allergy usually present
2 Onset after 45 usually	2 Onset before 45 usually
3 Cough precedes wheeze by several months	3 Cough usually comes with or follows the wheeze
4 Wheezing localized	4 Wheezing generalized
5 Diaphragm arched	5 Diaphragm apt to be flattened
6 No eosinophilia	6 Eosinophilia usual in sputum
7 Hemoptysis often	7 Hemoptysis rare
8 Marked weight loss and rapid downhill course	8 Weight and course about same

* From Moore M W Carcinoma of the lung with asthmatic symptoms Ann Allergy 3 271 1945

intervention is usually too late Moore's differential table is good but no one of his points is infallible

I Loeffler's syndrome is characterized by transient pulmonary consolidations with eosinophilia wheezing is often present and in some cases the symptoms are very suggestive of asthma Actually there is strong evidence for the belief that the condition is allergic Eosinophilia may be as high as 66% as emphasized by Loeffler[69] or even higher Symptoms usually clear spontaneously the x ray helps in showing the consolidations and their disappearances Skin tests may be positive as in a recent patient with strongly positive skin tests and freedom from consolidations since allergy measures were instituted over a year ago

J Tropical eosinophilia may be closely related and "occurs in the tropics especially in India. The chief symptoms are an insidious onset with malaise low grade fever headache and unproductive cough wheezing and dyspnea are often associated Leucocytosis (up to 60 000) and marked blood eosinophilia (up to 89%) are striking features Chest x ray films usually show fine mottling in both lungs One to six intravenous injections of Neoarsphenamine or other arsenical products cause prompt relief with disappearance of leucocytosis eosinophilia and the so called asthma No causative organisms have been found"[70]

K Periarteritis nodosa is a collagen disease that seems to have some relationship to allergy in general and to asthma in particular It involves small and medium sized arteries with periarterial infiltration by eosinophiles polynuclear cells and lymphocytes Occlusion frequently results and may occur anywhere in the body including the lungs Eosinophilia may reach 84 % or may be absent. Examination of blood vessels in a piece of calf muscle may be diagnostic More or less continuous administration of the corticosteroids may be life-saving

L Chronic cardiac decompensation may also confuse especially if it occurs along with bronchial asthma in an older patient who has some associated cardiorenal condition Noc

She went home but 18 days later she had an acute exacerbation She was returned to the hospital via ambulance but was dead on arrival

The diagnosis of this case provoked much discussion The persistent pulmonary infiltration ruled out bronchial asthma this despite the eosinophilia in the sputum The diagnosis of Boeck's sarcoid was suggested by several but against this were the facts that there were no x ray changes in the bones no skin or eye lesions no enlargement of the spleen and not enough reversal of the A G ratio

Other conditions were suggested but questioning of the patient had revealed that she operated a drill press in 1944-1945 and during this time she also worked with a buffing machine which gave off a great deal of dust Sometimes she wore a mask, sometimes she did not Because of this exposure and because of the chronicity of the process it seemed much more likely that she had developed silicosis of the lungs and from this cor pulmonale and resultant right heart failure This diagnosis was confirmed by the autopsy at which the patient was found to have anthracosilicosis of the lungs spleen and stomach and of the parabronchial pancreatic and renal lymph nodes—all this in addition to cor pulmonale and cardiac decompensation

D Asthmatic bronchitis may occur at any time of life but is especially common in the extremes of age It is characterized by attacks of cough wheezing fever leucocytosis, and increased sedimentation rate The attacks usually subside in a few days There is some argument as to whether or not this is a forerunner of true bronchial asthma Asthmatic bronchitis probably should be divided into two groups (1) those which are allergic from the start and have the characteristic allergic features e g family history of allergy response to epinephrine eosinophilia in the blood and sputum and positive skin tests In this group typical attacks of bronchial asthma will usually follow unless prompt preventive measures are instituted (2) In the other group infection is the main factor and true bronchial asthma rarely follows It is not always easy to differentiate these two groups when the attack occurs and the correct diagnosis may require time and study but allergy surveys should be made in both groups as future asthma may be prevented

F Bronchiectasis has been mentioned above It may occur with or without asthma It is characterized by attacks of cough with much sputum with or without dyspnea and/or wheezing showers of moist rales localized in one or more areas mild fever and hemoptysis in some and distinctive findings by x ray after instillation of radio opaque material In those cases in which bronchial asthma coexists eosinophilia in the sputum is usually found.

Case 6 Miss R C age nineteen white reported at the office October 1 1949 with asthma and nose trouble—duration three years She wheezed coughed and had some dyspnea especially on exertion Her nose was blocked a great deal along with a watery nasal discharge and frequent frontal headaches There were 11 600 leucocytes with 11 per cent blood eosinophilia and with 30 per cent eosinophils in the sputum

Skin tests were carried out by the scratch method supplemented by intradermal tests There were many positive skin tests and as a result she received injections for hyposensitization These consisted of extracts of grass pollen house dust feathers molds flaxseed and kapok

The interesting and unusual finding in this girl was the presence of clusters of bubbling rales heard below the left clavicle These rales were heard on every examination and were typical of those found in saccular bronchiectasis The first bronchograms failed to visualize the left upper lobe but on the second attempt the saccular bronchiectasis was beautifully shown Bronchoscopy revealed marked constriction of the left main bronchus as though a gland was pressing on both the upper and lower lobe orifices The bronchus was dilated twice and lobectomy was then carried out in June 1950 When the chest was opened the left upper lobe was found to be congenitally very small and was only as large as a lemon This lobe was removed and sections showed the saccular bronchiectasis along with chronic bronchitis and chronic interstitial pneumonitis There was no tissue eosinophilia The left lower lobe was quite large and filled most of the left chest cavity

The patient's progress has been most satisfactory Her cough and sneezing and frequent bouts of fever have disappeared although she still has mild rhinitis There is no further evidence of bronchial asthma and perhaps her wheezing was chiefly associated with bronchiectasis We never did hear the generalized wheezing which is so typical of true bronchial asthma

F Fungus diseases of the lung may also cause wheezing may occur at any age and may have a protracted course Suspicion should be aroused by the lack of the signs and symptoms of an allergic disease and the presence of diffuse pulmonary abnormalities on

fluoroscopy and chest x ray A history of having been in endemic areas e g the San Joaquin Valley (coccidiomicosis) or the Ohio or Missouri Valleys (histoplasmosis) is helpful and fungus skin tests are of value Finding the organisms in the sputum is diagnostic but this usually requires special culture media and well trained personnel

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* From Moore M W Carcinoma of the lung with asthmatic symptoms Ann *Allergy* 3 271 1945

intervention is usually too late Moore's differential table is good but no one of his points is infallible

I Loeffler's syndrome is characterized by transient pulmonary consolidations with eosinophilia wheezing is often present and in some cases the symptoms are very suggestive of asthma Actually there is strong evidence for the belief that the condition is allergic Eosinophilia may be as high as 66% as emphasized by Loeffler[29] or even higher Symptoms usually clear spontaneously the x ray helps in showing the consolidations and their disappearances Skin tests may be positive as in a recent patient with strongly positive skin tests and freedom from consolidations since allergy measures were instituted over a year ago

J Tropical eosinophilia may be closely related and "occurs in the tropics especially in India The chief symptoms are an insidious onset with malaise low grade fever headache and unproductive cough wheezing and dyspnea are often associated Leucocytosis (up to 60 000) and marked blood eosinophilia (up to 89%) are striking features Chest x ray films usually show fine mottling in both lungs One to six intravenous injections of Neoarsphenamine or other arsenical products cause prompt relief with disappearance of leucocytosis eosinophilia and the so-called asthma No causative organisms have been found"[30]

K Periarteritis nodosa is a collagen disease that seems to have some relationship to allergy in general and to asthma in particular It involves small and medium sized arteries with *periarterial infiltration by eosinophiles polynuclear* cells and lymphocytes Occlusion frequently results and may occur anywhere in the body including the lungs Eosinophilia may reach 84% or may be absent Examination of blood vessels in a piece of calf muscle may be diagnostic More or less continuous administration of the corticosteroids may be life saving

L Chronic cardiac decompensation may also confuse especially if it occurs along with bronchial asthma in an older patient who has some associated cardiorenal condition Noc

turnal insomnia may occur before edema of the feet, enlarged liver, moist rales at bases, etc A circulation time test should aid in separating the two conditions

TREATMENT OF BRONCHIAL ASTHMA

I. PREVENTIVE MEASURES

A Children of allergic parents are apt to develop allergic symptoms, including asthma They should therefore be shielded from the most common causes of attacks, e g, dogs, cats, orris root (certain cosmetics), feathers (pillows, comforters), fuzzy toys, excessive quantities of house dust, and large amounts of pollen as frequently found in vacant lots and in certain summer camps New foods should be introduced singly to see if symptoms result Cooked foods are less allergenic than raw foods and raw eggs may be disastrous The house should be spick and span, and a good vacuum cleaner is strongly advised, whisk brooms only spread dust [31] Rubber or Dacron pillows and mattresses are recommended, also rubber-filled furniture and avoidance of thick drapes and carpeting

B Mild allergic symptoms are apt to occur early in these children, e g, eczema, frequent bronchitis, hay fever, rhinitis, wheezing, or various gastrointestinal "upsets." Complete skin tests should be done at once, followed by elimination of offending allergens Hyposensitization may also be necessary and should not be delayed. It is easier to prevent chronic asthma than to cure it. *Children rarely "outgrow" asthma*

C Allergic individuals and their children should avoid dusty occupations (see Table II), especially farmer, baker, furrier, grain mill worker, upholsterer, and domestic

D Allergic individuals should not intermarry, but this advice is easier to give than to follow

E Hygienic measures are important, especially as regards avoidance of persons with ordinary "colds,"—"colds" are very apt to precipitate severe asthma in allergic individuals

II. SPECIFIC TREATMENT

Excellent results are usually obtained in those patients whose offending allergen or allergens have been removed In some, complete avoidance is impossible and hyposensitization is also necessary Both of these methods are highly important By elimination we avoid the specific allergens Hyposensitization is an attempt, usually successful, to raise the patient's resistance so that he can withstand *average* amounts of the offending allergen

A Avoidance If there were no exposure, there would be no attacks Complete avoidance leads to complete relief from symptoms, i e, "cure" from a clinical point of view in paroxysmal asthma Such elimination also is valuable in chronic asthma, but complete relief should not be expected in patients who have already developed emphysema and chest deformities From an immunologic point of view, "cure" is rare even in paroxysmal cases because recurrence often follows re exposure, e g, to a dog or cat

The patient is given written directions as to avoidance of offending foods and inhalants Care is emphasized and firmness is often necessary to actually see that the patient follows orders Many patients do not want to part with the family dog or cat, and others do not clean their homes from an allergic point of view If inhalation of house dust and/or feathers and kapok causes attacks of asthma, the homes must be made as free from these allergens as possible Good vacuum cleaners with attachments are essential Rubber bedding or dust-proof zippered covers are always ordered The bottoms of all soft furniture are boarded with linoleum or plastic so that dust cannot fall to the floor These are a few of the necessary measures. House dust is not only an allergen, but can also act as a disease carrier, as described by A H Unger [32]

In allergy to foods the patient must completely avoid the particular food and all foods which contain it, e g, wheat and all wheat-containing foods Half-way measures frequently fail If a patient is allergic to one food of a particular botanical family, e g,

citrus fruits it is usually advisable to avoid the other members of that family

B Hyposensitization (desensitization) consists of injections of increasing amounts of extracts of important allergens which cannot be avoided e g house and occupational dusts pollens fungi animal danders orris root and cottonseed The results are usually good The oral method is rarely used

The technique and indications are described in many books and articles The beginning dilution is based on the degree of sensitivity of the patient to the particular allergen e g ragweed or horse dander The details vary with different allergists but most men raise the dosages about twice a week until local reactions occur Great care is necessary to prevent constitutional reactions e g asthma rhinitis urticaria and shock The injections are usually necessary for a long time but the intervals can be lengthened to approximately every two to four weeks

Results from hyposensitization (desensitization) are discussed in a recent article [33]

Even though hyposensitization has now been in use for many years I still cannot give my results with great accuracy especially because I still have no definite technique by which to estimate such results It is true that the size of skin test reaction almost always lessens with injections and that this decrease is more or less proportionate to clinical results But even in patients in whom results have been brilliant intradermal skin tests are still apt to be positive Furthermore with hyposensitization tolerance to the extracts usually continues to increase at least to a certain level

Clinically one is on firm ground Years of experience have shown that in most cases hyposensitization leads to an increase of the patient's resistance so that he can withstand ordinary exposure to his offending allergen or allergens Patients with pollen allergy usually receive fair to excellent results Most such patients with hay fever have relatively few symptoms except during the days when pollen counts are very high

Happily most patients with asthma caused by pollen obtain excellent results usually their asthma is either eliminated or becomes minimal but they must continue to have injections for many years

Results from injections of mold extracts are probably not as good as those from injections with pollen On the other hand results are usually excellent with injections of other inhalant materials especially house dust danders feathers and smuts Occupational dust extracts also give good results provided exposure is not excessive as it would be in the case of bakers and grain mill workers

III TREATMENT OF CONTRIBUTORY FACTORS

This consists chiefly of efforts to avoid those influences already discussed e g inhalation of various kinds of dusts fumes bacteria and viruses Psychogenic and endocrine factors must also be combatted as they may aggravate or incite attacks in allergic persons who are also exposed to exciting allergens Sometimes the influence of psychogenic and infectious factors and of exposure to fumes are very important Tobacco smoke, for example is to be avoided by all asthmatics

IV SYMPTOMATIC TREATMENT

While nonspecific treatment is important it gives less favorable and less permanent results than can be secured from elimination of the specific factor with or without hyposensitization This symptomatic treatment consists of measures used both during and between attacks

There are many available therapeutic measures but the authors recommend the following

A Reassurance of the patient is the most important single measure The attacks may frighten the patient (and the family) Tell him that the attack will subside (and it almost always does) Death is rare in uncomplicated asthma (unless morphine has been used) The calm confident attitude of the physician is very valuable to the patient Urbach[34] was correct in saying that "the asthma doctor must and dare not forget that his own quiet deliberate and reassuring manner and his absolute conviction that almost all cases of asthma can be cured constitutes one of the most important prerequisites for success"

B Restrict the patient's activity but only when asthma is present The patient is already short of oxygen needless exertion only aggravates During free intervals patients especially children should be encouraged to exert themselves to the point where symptoms begin

C. The patient's room should be as dust-free as possible, with bare floor or linoleum, dust-proof bedding covers, clean curtains, and no animals. If inhalation of pollen and/or fungi is a factor the windows must be shut or an air filter should be installed in the window.

The Chicago Wesley Memorial Hospital has twelve beds especially designed to take care of severe asthmatic patients. Filters clean the air, the bedding is rubber, linoleum covers the floor, the furniture is steel and synthetic leather, and the rooms are practically dust free. Almost every patient whose asthma is due to inhalation of an allergen is quickly relieved in such a room. If his symptoms do not disappear in four to seven days he is probably allergic to a food or has some bacterial or other complication. Every hospital should have similar rooms for allergic patients.

D. Aminophylline is probably better than epinephrine except in children. It does not excite the patient, raise his blood pressure or cause tachycardia. When given intravenously it acts quickly and usually gives prompt relief. We recommend 0.24 gm. ($3^3/_4$ grains) given slowly with a 10 cc. eccentric all glass syringe. These injections can be repeated 2 to 3 times a day, if necessary. If the patient is in a hospital the initial dose of 0.24 gm. should be followed by 0.48 gm. mixed with a liter of 5% glucose at 60 drops per minute. This liter mixture should be given daily for 3 to 4 days. Aminophylline is also useful when given rectally (for adults 10 grains dissolved in 20 cc. tap water), or $7^1/_2$ grain (0.50 gm.) suppositories. Aminophylline by mouth is useful, but acts more slowly.

E. Epinephrine (1:1000) is the symptomatic treatment of choice in children (0.10 to 0.20 cc.), and is also of great value in adults (0.25 to 0.50 cc.). Besides the subcutaneous use of a 1:1000 dilution, it can be used as a nebulizer (1:100) by inhalation, or even intravenously 1 cc. of the 1:1000 solution in a liter of 5% glucose in water. Used intravenously it is often included in a liter of fluids to which 20 cc. of aminophylline and perhaps 20 units of ACTH have been added. By this route it is effective even in those patients who are supposedly "epinephrine-fast." We have also found a 1:200 solution in glycerine (Sus-Phrine)® valuable for prolonged action; it has the advantages over epinephrine in oil in that it can be given subcutaneously and can be mixed with the 1:1000 dilution of epinephrine, thus eliminating one injection in those patients in whom both immediate and prolonged relief of wheezing is desired.[15]

F. Ephedrine in doses of $^3/_8$–$^1/_2$ grain (25–32 mg.) orally, is useful in moderate and mild asthma. It has epinephrine-like effects, and should be combined with a sedative, e.g., phenobarbital. Precautions are similar to those with epinephrine.

G. Oxygen inhalation is indicated in cyanosis or great weakness. It is not of much avail in uncomplicated asthma, and care must be used in patients with severe emphysema. Helium may be added but is seldom used.

H. Glucose is a valuable food and perhaps has a more important role in asthma. It is known that epinephrine forces glucose from the liver, hence patients who have received much epinephrine need glucose. We therefore give each patient 5 ounces daily of glucose suspended in a quart of fruit juices.

I. Iodides are invaluable in the treatment of asthma and act by loosening the sputum. They may be combined with apomorphine, a good expectorant, as follows:

Apomorphine hydrochloride	grains 2
Potassium iodide	drams 5
Syrup Cherry q.s.a.d.	ounces 4

Sig. Teaspoonful four times daily.

J. Syrup of ipecac, until emesis occurs, is extremely valuable in relieving asthma in children. Retching brings up inspissated plugs of mucus from the small bronchioles, thus eliminating areas of atelectasis, increasing effective oxygenation of the lungs, and alleviating symptoms.

K. Sedation is the foremost stumbling block in the treatment of bronchial asthma. Both the patient and the family are often noisy and upset, and the temptation to use heavy sedation is sometimes overwhelming. We feel that this temptation must be resisted, and that nothing stronger than small amounts of Benadryl® or Phenergan® should be used. We strongly recommend 1 to 2 oz. whiskey at night, plus 10 grains of aspirin (unless contra-

indicated by hypersensitivity) We do not agree with some allergists who use small amounts of Demerol[5] (e.g. 50 mg.) All agree that *morphine must never be used* By depressing respiration and lessening the cough reflex *morphine may well result in respiratory* acidosis suffocation and the death of the patient Tranquilizing drugs may prove useful in asthma but they await further evaluation

L The use of *ether* by enema (in mineral oil) or as a general anesthetic will usually terminate an attack but has fallen into disuse since the advent of the steroids

M Chemotherapy is valuable in those asthmatics *who have an infectious element to their* asthma When such a patient has crepitant rales fever leukocytosis an elevated sedimentation rate and perhaps some mottling on the chest x ray antibiotics are indicated and often give dramatic results Also children with recurrent infections and resultant asthma are often benefitted by long *term tetracycline* therapy throughout the winter months

N *Gamma globulin is also used prophylactically* in children whose asthma is related to repeated infections It is used despite the fact that they usually have normal amounts of gamma globulin in their blood and sometimes yields dramatic results in resistant cases It is expensive however and rather painful on administration Much work needs to be done along these lines

O Bronchoscopic *aspirations may be lifesaving* in patients who cannot cough up *their own sputum* In severe asthma however the bronchoscopist often cannot aspirate the tenacious sticky sputum

P Last and definitely not least are the *steroids* Without them life would be far more trying both for the physician and the patient They are a two edged sword being miraculous and often life saving on the one hand and potentially deadly on the other In the treatment of the acutely ill asthmatic we add 20 units of ACTH to each liter of 5% glucose in water as well as the above *mentioned 20 cc* of aminophylline and give each bottle over an 8 hour *period When the patient's symptoms* are alleviated we stop the intravenous drip and give 40 units of ACTH gel intramuscularly twice a day followed by gradually *decreasing doses of the gel over the next several* days For the attacks not quite severe enough to merit *hospitalization* we use prednisone starting with 30 to 40 mg a day and decreasing the dosage fairly rapidly There are some patients whom we have been forced to maintain on 5 to 10 mg a day for several years as any lowering of dosage below this level results in severe asthma The contra*indications for the use of steroids in asthma* are the same as in any other disease being primarily a history of an ulcer or ulcer like pains tuberculosis and psychosis All contraindications are relative of course and we have used cortico steroids successfully in patients with active tuberculosis who seemed to be dying of bronchial asthma Also it must be remembered that any patient who has been on long *term steroid therapy may need extra adrenal* hormones should they require surgery

As previously mentioned steroids are also valuable in giving symptomatic relief without the use of sympathomimetic or antihistaminic agents thus preparing the patients for skin tests which could not be done accurately otherwise The steroids interfere with delayed skin testing e g tuberculin and histoplasmin but *not with the immediate reacting type e g rag*weed and dust

Finally it must be understood that steroids do not "cure" asthma and are only useful for symptomatic relief They are adjuvants to the general management of the patient but in no way alter the basic concepts of treatment of the asthmatics These concepts are the discovery of the causes of the attacks elimination of the causes where possible and hyposensitization where not possible Steroids are a godsend in the critically ill patient, but are still "the tail of treatment that should not be *allowed to wag the dog*"

RESULTS OF TREATMENT IN BRONCHIAL ASTHMA

Results in paroxysmal asthma are usually brilliant if the above care and precautions are observed This applies especially to those patients who have had a careful history and

TABLE VI

RESULTS OF TREATMENT IN 459 CASES OF BRONCHIAL ASTHMA (1)

Age at Onset	Paroxysmal: 100% "Cured"	Improved	Unimproved	Dead	Chronic: 100% "Cured"	Improved	Unimproved	Dead
0–9	55	81	5	3	—	23	9	5
10–19	9	29	6	—	2	13	9	4
20–29	17	27	4	2	—	8	10	4
30–39	8	17	5	1	—	11	7	6
40–49	4	17	—	3	2	7	9	11
50–59	—	2	1	2	—	9	4	4
60–69	—	—	—	—	—	1	—	3
Totals	93	173	21	11	4	72	48	37

TABLE VII

SUMMARY OF RESULTS OF THERAPY IN 459 CASES OF BRONCHIAL ASTHMA (1)

	100% ("Cured")	Improved	Unimproved	Dead	Total
Paroxysmal	93 (31 2%)	173 (58 0%)	21	11	298
Chronic	4 (2 4%)	72 (44 7%)	48	37	161
Total	97	245	69	48	459

examination and who have also had complete skin tests and laboratory studies all this followed by avoidance of offending allergens, with or without specific hyposensitization

In chronic asthma, however, complete relief from symptoms is uncommon because of irreversible changes, e g , emphysema

The results are therefore much better in children as shown in Tables VI and VII

The average internist, including those who specialize in chest diseases, has more or less neglected the field of allergy He is apt to try to find the cause by history and clinical tests alone, and to disregard skin tests Skin tests by themselves, however, are useless Their results must have clinical correlation The best results are obtained by a combination of a careful history, examination and laboratory tests, plus an intelligent allergy survey, including thorough skin tests

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CHAPTER 13

Pulmonary Fibrosis

ANDREW L. BANYAI, M.D.

SEVERE damage to the specific elements or to the supportive frame work of the lung is often times repaired by the formation of fibrous tissue. Thus alveoli filled with exudate are occupied by fibroblastic invasion and proliferation. An overgrowth of connective tissue takes the place of functional units of the lung and causes obliteration of the corresponding blood vessels and lymphatics. The fibrous tissue is fleshy, dense, tough and airless, that is, it represents areas of no functional value.

Relative to classification, pulmonary fibrosis may be predominantly parenchymal (intra alveolar), interstitial or the combination of the two. It may be found in one or both lungs. *In either instance, the involvement may be* limited to a lobe, segment, subsegment or smaller area. It may be solitary or multiple. It appears in round, oval, triangular, nodular or plate-like form or it may show an irregular pattern.

Most instances of pulmonary fibrosis are attributable to foregone pathological changes in *the lung itself. In some cases, however, fibro*sis is a manifestation of a systemic affection as seen in collagen diseases (scleroderma, dermatomyositis, lupus erythematosus, polyarteritis) rheumatic fever, syphilis, polycythemia vera. Sometimes, instances of xanthomatosis and primary pulmonary amyloidosis are associated with extensive pulmonary fibrosis.

Lewin and Heller observed pulmonary fibrosis in 8% of patients with scleroderma. The pathologic picture is dominated by extensive proliferation of connective tissue, diffuse alveolar fibrosis, thickening of the alveolar walls and formation of dense fibrotic nodules from 1 to 15 mm in size.

Specific pneumonitis occurs in from 1 to 10% of patients suffering from rheumatic fever. Fibrosis may be pronounced in the subacute and chronic types. *It is noted in the* form of unevenly distributed, diffuse interstitial changes.

Nowadays syphilis of the lung is a rarely seen clinical entity. *Fibrosis is a common* manifestation of various forms of this condition. *Regardless of their size gummas are usu*ally surrounded by sclerotic changes. In chronic interstitial pneumonitis, fibrosis shows a radiating pattern which extends from the hilum along the bronchovascular structures. There is likely to be extensive fibrosis of the interlobar and thoracic pleura, *with a tendency* to contraction of the respective hemithorax. *Massive fibrosis may result from syphilitic lo*bar pneumonia and bronchopneumonia. Contrary to earlier contentions, it is the consensus that Ayerza's syndrome, with its pronounced peribronchial and perivascular fibrosis may be brought about by a number of pathogenic factors other than syphilis.

Polycythemia vera may lead to the develop*ment of pulmonary fibrosis through the organ*ization of perivascular hemorrhages or infarcts.

Pulmonary fibrosis may be encountered in some cases of aplastic anemia and also, in leukemia.

In contrast to the comparatively small number of essential (idiopathic, genuine) pulmonary fibrosis, known as Hamman Rich syndrome, fibrosis of the lung is commonly observed as a sequel to identifiable pulmonary diseases. In this category belong infections (*bacterial, viral, rickettsial, protozoan, para*sitic), injury resulting from the inhalation of noxious fumes, gases and dusts and that which is brought about by heavy irradiation *with* x ray or radium. Also, in this connection, mention should be made of other possible causal

sources such as cardiovascular disturbances (severe pulmonary congestion infarction) allergy mechanical trauma Moreover pulmonary fibrosis may develop in areas of atelectasis with superimposed infection and also in patients with pulmonary edema due to malignant hypertension or renal failure Furthermore pulmonary fibrosis may originate from the aspiration of mineral oil when used as a cathartic nose drops or spray Similar reaction follows aspiration of animal fats (cream cod liver oil) Instances of pulmonary fibrosis have been reported in which the condition resulted from the prolonged administration of hexamethonium for the treatment of hypertension

Auerbach and his associates expressed the view that the use of sulfonamides and antibiotics may result in pulmonary fibrosis They assume that these drugs interfere with the protective invasion of leucocytes in the involved areas of the lung Also it is thought that these drugs retard or prevent the proteolytic function of leucocytes which reach the site of a pneumonic process Consequently the inflammatory exudate is penetrated by fibroblasts and becomes organized They pointed out on the basis of their histological observations that this sort of fibrotic organization may be detectable within seven eight and nine days after the onset of pneumonia

Discussion of the pathologic and clinical aspects of occupational fibrosis of the lung is presented in another chapter

In view of the increasing use of radiation energy in the treatment of tumors of the breast lung mediastinum and esophagus the possibility of consequent pulmonary fibrosis deserves due attention The main factors which have a bearing on the development of fibrotic changes are the amount of radiation energy used the size of portals of irradiation the age of the patient the presence or absence of arteriosclerosis lung infection and individual sensitivity Pathologic alterations secondary to radiation vary from fibrillar hyalinization thickening of the alveolar walls peribronchial and perivascular sclerosis to massive fibrosis of the lung As a rule there is concurrent fibrosis of the pleura with adhesions between its visceral and parietal surfaces and also with pleuropericardial adhesions

In chronic pneumonitis of the cholesterol type as reported by Waddel and his coworkers and by Robbins and Sniffen deposition of large amounts of cholesterol was followed by extensive interalveolar and interlobular fibrosis The involvement may occupy the entire extent of one lobe or only one or more of its segments

In reference to cardiovascular diseases two items are to be mentioned (1) Tissue necrosis of variable extent is the usual sequel of pulmonary infarction This in turn leads to the development of localized fibrosis of linear appearance or of irregular shape (2) Long standing mitral stenosis as well as long continued failure of the left ventricle are bound to cause widespread interstitial pulmonary fibrosis secondary to chronic passive congestion

Fibrous thickening of the alveolar walls perialveolar capillaries smaller arteries and veins together with interstitial fibrosis are characteristic components of essential pulmonary hemosiderosis (idiopathic progressive brown induration of the lung Ceelen Gellerstedt disease) This is an uncommon disease of grave prognosis which has been observed in infants and children

Another disease of infancy and childhood mucoviscidosis also known as fibrocystic disease of the pancreas is associated with complex pathologic changes in the lung such as mucopurulent bronchitis bronchiectasis bronchiolectasis bronchopneumonia and fibrosis The latter may be represented by widespread peribronchial or patchy parenchymal localization

Xanthomatosis (histiocytosis reticuloendotheliosis eosinophilic reticuloendotheliosis lipoidosis lipoid histiocytosis lipoid granulomatosis eosinophilic granulomatosis) may have pulmonary manifestations In the late stages of involvement extensive interstitial fibrosis is readily detectable on roentgenologic examination Emphysema is a usual concurrent finding The hilar lymph nodes may be enlarged The etiology of this disease is a much debated issue Thannhauser maintains that the underlying cause is a localized intra

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unction may be handicapped by dislocation f the heart toward the involved side when t is associated with kinking of the pulmonary vein or other mechanical impediments to the free flow of blood

DIAGNOSIS

Minor pulmonary fibrosis as a rule is latent and asymptomatic throughout life Even ibrosis of moderate extent may exist without ymptoms only to be detected on routine hest x ray examination

Findings on physical examination depend upon the extent of the disease and upon the presence or absence of complications such as atelectasis bronchiectasis superimposed in fection (bronchitis pneumonia) broncho pasm emphysema and cor pulmonale

When large areas of the lung are occupied by cirrhotic fibrosis corresponding changes in the contour of the overlying chest wall are observed Parts of the thorax or the entire hemithorax may be contracted with retraction of the supraclavicular fossa increased declivity of the respective ribs together with decreased respiratory motion of the chest wall On percussion one may note lack of normal resonance and reduction or absence of the respiratory excursions of the diaphragm Breath sounds are diminished absent or distant bronchial in character Rales are frequently heard over the involved area Their number and type ("moist" or "sonorous) are depend ent upon bronchial structural changes and presence or absence of infection in the lower respiratory tract

Roentgenographic and fluoroscopic examina tions are indispensable for the accurate assay ing of the patient s condition Pathologic al terations in the shape and size of the affected hemithorax are easily discernible There is increased slanting of the ribs The inter costal spaces are narrowed There may be scoliosis of the spine One or both hemi diaphragms are high and more or less fixed The trachea and the heart may be displaced toward the diseased side Cardiomegaly due to cor pulmonale may be noted In cases of pronounced pulmonary cirrhosis one finds not only compensatory emphysema but also mediastinal herniation of the uninvolved lung

In the lung field of the implicated side fibrosis may appear as web like net like shadow sharply demarcated strands which radiate from the hilum toward the periphery widely distributed small nodular opacities moderate or large sized solitary or multiple oval or irregular shaped dense more or less homogeneous shadows of segmental or lobar distribution One may find a homogeneous density occupying practically an entire hemithorax

Other possible findings are thickening of the peripheral interlobar and mediastinal pleura displacement of the hilar structures and of the interlobar fissures In some in stances reversible or irreversible forms of pneumocele are found

In diagnostic work full advantage should be taken of comprehensive x ray examination including roentgenograms taken in oblique lateral and lordotic positions tomograms bronchograms, angiopneumography films taken in full inspiration and expiration Car diorespiratory function studies may reveal valuable contributory data Due attention should be given to bacteriologic cytologic and chemical examination of the sputum Sero logic and hematologic findings may have an important bearing on the issue Broncho scopic examination aspiration biopsy scalene node biopsy or exploratory thoracotomy may be required for precise diagnosis

The following conditions should be con sidered from the standpoint of differential diagnosis pulmonary infections primary and metastatic neoplasms of the lung and other thoracic organs and structures atelectasis infarction collagen diseases congenital cysts filled with fluid hypogenesis or agenesis of one lung pulmonary edema arteriovenous fistula of the lung ectopic kidney or spleen aspirated foreign body diverticulum of the esophagus diaphragmatic hernia encapsulated

cellular enzymatic disorder of the reticulo endothelial cells This results in the formation of anamalous lipids which constitute the *pathologic essence of xanthomatosis*

Fibrosis is one of the cardinal aspects of *middle lobe syndrome* This condition is brought about by occlusion of the bronchus *to this lobe by enlarged lymph nodes* neoplasm or by other intrinsic or extrinsic factors *Atelectasis pneumonitis are the other features* of this entity

Renal failure resulting *from glomerulonephritis* or nephrosclerosis may be associated with uremic lung The *subsequently de*veloping pulmonary fibrosis is either interstitial or parenchymal

During the reparative phase of rheumatic pneumopathies fibrosis may appear in the form of diffuse interstitial sclerosis nodular or patchy conglomeration of fibrous tissue which occupies sites of the affected parenchyma Ehrich and McIntosh described bronchiolitis obliterans secondary to fibrotic alterations in this condition Auerbach and his associates noted that in histological specimens *foci of organization were indistinguishable* from the Masson body found in rheumatic *pneumonia*

SYMPTOMS

Symptoms of pulmonary fibrosis are predicated upon its extent and location with particular reference to obliteration of the lower air passages vascular structures of the lung and also pleural adhesions Moreover symptoms may arise from pathologic changes secondary to fibrosis especially atelectasis superimposed bronchopneumonia bronchiectasis emphysema and cor pulmonale

Lesions of small size regardless of their *situation are likely to remain symptomless* throughout life Extensive fibrosis on the *other hand is bound to bring the patient to* the physician with complaints of cough pain in the chest and dyspnea Without associated infection cough is slight hacking unproductive but persistent It gives the impression of a cold in the chest which is difficult to control Expectoration of mucoid or mucopurulent sputum is common with superimposed infection particularly when there is secondary bronchiectasis

The patient may complain of slight or pronounced pulmonary hemorrhage *which may* be recurrent Pulmonary hemorrhages originate *from bronchial mucosal inflammation* with or without ulceration or from dilatation of pulmonary blood vessels

Pain and tightness in the chest are caused by involvement of the pleura dislocation of some of the thoracic organs and structures and in some instances from reflex bronchospasm

Considerable loss of alveolar surface area occlusion of numerous bronchi obliteration of pulmonary blood vessels are bound to result in dyspnea Extensive pleural and pleuropericardial adhesions dislocation of the heart and the mediastinal large vessels upward displacement and fixation of the diaphragm deformity and contraction of the chest wall interfere with cardiorespiratory *function and* thus lead to shortness of breath

*In a great many of my patients with pul*monary fibrosis I have observed that the *severity of dyspnea* was far greater than anticipated from the extent of pulmonary involvement Pertinent clinical studies revealed that much of the dyspnea in these instances was attributable to reflex bronchospasm provoked by fibrosis Awareness of this possibility of course has important therapeutic implications It is well to emphasize at this time that there are pronounced variations in the bronchospasmogenic response of various *individuals*

Widespread pulmonary fibrosis is a common *cause of chronic cor pulmonale* Several factors are responsible for its causation (1) Pulmonary vascular and perivascular sclerosis interferes with blood circulation by narrowing or obliterating the vascular bed (2) Respiratory and ventilatory insufficiency inevitably follows replacement of large number of alveoli by scar tissue Stenosis or occlusion of *bronchi* by constricting fibrosis concurrent atelectasis aggravate *this situation* (3) *Normal* cardiac

function may be handicapped by dislocation of the heart toward the involved side when it is associated with kinking of the pulmonary vein or other mechanical impediments to the free flow of blood.

DIAGNOSIS

Minor pulmonary fibrosis as a rule is latent and asymptomatic throughout life. Even fibrosis of moderate extent may exist without symptoms, only to be detected on routine chest x-ray examination.

Findings on physical examination depend upon the extent of the disease and upon the presence or absence of complications such as atelectasis, bronchiectasis, superimposed infection (bronchitis, pneumonia), bronchospasm, emphysema and cor pulmonale.

When large areas of the lung are occupied by cirrhotic fibrosis, corresponding changes in the contour of the overlying chest wall are observed. Parts of the thorax or the entire hemithorax may be contracted, with retraction of the supraclavicular fossa, increased declivity of the respective ribs, together with decreased respiratory motion of the chest wall. On percussion, one may note lack of normal resonance and reduction or absence of the respiratory excursions of the diaphragm. Breath sounds are diminished, absent or distant bronchial in character. Râles are frequently heard over the involved area. Their number and type ("moist" or "sonorous") are dependent upon bronchial structural changes and presence or absence of infection in the lower respiratory tract.

Roentgenographic and fluoroscopic examinations are indispensable for the accurate assaying of the patient's condition. Pathologic alterations in the shape and size of the affected hemithorax are easily discernible. There is increased slanting of the ribs. The intercostal spaces are narrowed. There may be scoliosis of the spine. One or both hemidiaphragms are high and more or less fixed. The trachea and the heart may be displaced toward the diseased side. Cardiomegaly due to cor pulmonale may be noted. In cases of pronounced pulmonary cirrhosis one finds not only compensatory emphysema but also mediastinal herniation of the uninvolved lung.

In the lung field of the implicated side, fibrosis may appear as weblike, netlike shadow, sharply demarcated strands which radiate from the hilum toward the periphery, widely distributed small nodular opacities, moderate or large sized solitary or multiple oval or irregular shaped dense, more or less homogeneous shadows of segmental or lobar distribution. One may find a homogeneous density occupying practically an entire hemithorax.

Other possible findings are thickening of the peripheral, interlobar and mediastinal pleura, displacement of the hilar structures and of the interlobar fissures. In some instances reversible or irreversible forms of pneumocele are found.

In diagnostic work full advantage should be taken of comprehensive x-ray examination, including roentgenograms taken in oblique, lateral and lordotic positions, tomograms, bronchograms, angiopneumography, films taken in full inspiration and expiration. Cardiorespiratory function studies may reveal valuable contributory data. Due attention should be given to bacteriologic, cytologic and chemical examination of the sputum. Serologic and hematologic findings may have an important bearing on the issue. Bronchoscopic examination, aspiration biopsy, scalene node biopsy or exploratory thoracotomy may be required for precise diagnosis.

The following conditions should be considered from the standpoint of differential diagnosis: pulmonary infections, primary and metastatic neoplasms of the lung and other thoracic organs and structures, atelectasis, infarction, collagen diseases, congenital cysts filled with fluid, hypogenesis or agenesis of one lung, pulmonary edema, arteriovenous fistula of the lung, ectopic kidney or spleen, aspirated foreign body, diverticulum of the esophagus, diaphragmatic hernia, encapsulated

pleural effusion thickening of the pleura paravertebral abscess massive enlargement of the hilar lymph nodes pericardial fat pad organizing intrapleural fibrin bodies

TREATMENT

Although pulmonary fibrosis is a permanent and unalterable condition *nihilistic attitude is not justifiable in the management of these cases There are means and ways of inestimable value for symptomatic alleviation* Cough can be effectively controlled by dihydrocodeinone bitartrate (hycodan dicodid mercodinone) codeine and other suitable opium derivatives or by some of the synthetic nonnarcotic cough sedatives In instances with pronounced bronchospastic dyspnea great benefits may be derived from the administration of bronchospasmolytic drugs particularly those with epinephrine like and ephedrine like action or with cholinergic influence Theophylline with ethylene diamine is effective for this purpose *All of these drugs can be given without harmful reaction for an extended period of time* In cases with severe bronchospasm prednisone or prednisolone *may* bring about salutary results *Preferably they* are used only for short periods of time

Smoking should be prohibited so as to avoid "smoker s syndrome pharyngitis laryngitis *tracheitis bronchitis and bronchiolitis* Other harmful effects of inhalation of tobacco smoke include in reference to this subject broncho spasm interference with normal bronchial peristalsis and retardation of ciliary function of the bronchial mucosa The two latter seriously interfere with spontaneous cleansing of the lower air passageways

Prevention and prompt treatment of infections of the lower respiratory tract are of prime importance

Some patients derive satisfactory though temporary relief from dyspnea by intermittent positive pressure breathing of oxygen

Treatment of complicating bronchiectasis and emphysema is outlined in other chapters

Due attention to secondary heart failure is mandatory

Surgical intervention may be called for in certain types of pulmonary fibrosis Harte reports a pertinent case A patient of his developed severe chest pain following post operative pulmonary infarction The pain was exasperating and persisted for a period of $3^1/_2$ months Roentgenogram of the chest showed a moderately dense shadow which occupied an area corresponding to the right lower lobe This finding was interpreted as thickening and extensive adhesion of the visceral pleura to the chest wall The surgical intervention consisted of severance of these adhesions in anticipation that the continuous tug caused by the pleural symphysis would be eliminated The operation was followed by complete relief from chest pain

HAMMAN-RICH SYNDROME

(Diffuse Fibrosing Interstitial Pneumonitis)

In 1935 Hamman and Rich first published their observations on an unusual pulmonary disease characterized by rapidly progressing diffuse interstitial fibrosis Since then a number of confirmatory reports appeared in the medical literature Its etiology has not been definitely established It is assumed to be of viral origin Instances are on record of its occurrence in siblings without close contact for an extended period of time This is suggestive of possible congenital familial predisposition

Contrary to earlier reports that the disease runs an acute course and terminates fatally cases have been observed in which the condition lasted for seven years or the patient survived for a long time

The condition is characterized by pronounced thickening of the alveolar walls together with sclerosis of the supportive tissues

of the lung and with the formation of consolidation of considerable size in all lobes. The pathologic process does not appear in all parts of the lung at the same time but shows progressive extension.

The development of this disease is as a rule not associated with severe toxic symptoms. Some patients may have subfebrile temperature or an irregular fever which may reach 103°F. The onset may be insidious or it is signalized by cough, chest pain and dyspnea. The latter is noticed on exertion only in the early stages of the disease. Subsequently, however, shortness of breath becomes increasingly worse. Thus patients are dyspneic, even orthopneic while staying in bed. Cough may persist, become harassing and may be productive of small amounts of mucoid or mucopurulent, greenish yellow, tenacious, occasionally blood tinged sputum. Fibrinous pleurisy or straw colored pleural effusion may develop during the course of illness.

On physical examination the patient appears cyanotic, having rapid labored respiration. Initially findings are scanty on auscultation. In the late stages breath sounds are harsh and fine or course moist rales and sonorous rales are audible over wide areas of both lungs, particularly at the bases. With progression of the pulmonary involvement signs of cor pulmonale develop, namely cardiomegaly, engorgement of the veins of the neck, hepatomegaly and pitting edema of the legs. Corresponding electrocardiographic signs are noted. The pulmonary second sound is accentuated. Pleural friction sound may be audible or findings are detected which are characteristic of pleural effusion.

Roentgenogram of the chest shows fine reticulation and small nodular densities throughout both lungs. The roentgenographic appearance may be suggestive of pulmonary edema. Also one may note confluence of minute nodular shadows into patchy irregular shaped densities. Perifocal emphysema is common. One may detect evidence of bronchiolectasis. The hilar vascular markings are prominent and the right ventricle of the heart is likely to be found enlarged. In general x ray picture of the chest may closely resemble a number of conditions such as miliary tuberculosis, miliary bronchopneumonias, miliary abscesses, meliodosis, miliary gummas, tropical eosinophilosis, dermatomyositis, scleroderma, silicosis, berylliosis, metastatic carcinoma, pulmonary adenomatosis, lymphatic leukemia and Hand Schuller Christian disease.

Laboratory findings are noncontributory to diagnosis. Bacteriologic studies on the sputum, fasting gastric contents as well as blood cultures and serologic tests are negative. There is a slight or moderate leucocytosis. Late in the course of the disease the white blood cell count may be high on account of intercurrent infection.

Lung biopsy is the only means to establishing the correct clinical diagnosis.

Symptomatic improvement, even some retrogression in the pulmonary findings may result from the administration of corticosteroids. Discontinuance of this medication is likely to be followed by flare up and rapid progression of the disease. Palliative measures are to be used promptly and adequately so as to offer the patient symptomatic relief through the alleviation of cardio pulmonary failure.

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CHAPTER 14

Emphysema

ANDREW L BANYAI M D

A NUMBER of technical terms have been applied to the condition discussed in this chapter of which hypertrophic emphysema is the most commonly used It is also known under the following names genuine emphysema idiopathic emphysema diffuse vesicular emphysema obstructive emphysema dystrophic emphysema pulmonary hypertrophy pulmonary dilatation chronic large lung and pneumonectasis Some years ago I proposed the term pseudohypertrophic emphysema In support of this new nomenclature I wish to offer the following explanation "Hypertrophy of the lung in this type of emphysema is far from being similar to muscular hypertrophy of the extremities seen in men engaged in athletics or in occupations which entail heavy physical work Although in genuine emphysema the lung is larger than normal there is neither an increase in the number of functionally competent alveoli nor a proportionate augmentation in the number size or functional capacity of corresponding capillary vessels On the contrary the distinguishing cardinal characteristics of pseudohypertrophic emphysema are (1) distention and destruction of alveoli which are the angio respiratory end organs of the lung (2) extensive destruction of perialveolar peribronchial and peribronchiolar elastic fibers Compensatory emphysema secondary to extensive pleuropulmonary disease is bound to result in identical changes in the long run The same holds true of space occupying tumors and pathologic alterations in the mediastinum and other thoracic structures and of pronounced deformity of the chest wall

The term emphysema is derived from the Greek words which mean "in" and blow Applied to the lung this term signifies inflated lung According to the derivation of this term senile emphysema is a misnomer for in this condition the lung is small with the exception of the Kountz Alexander type of senile emphysema On postmortem examination when the chest is opened the lung collapses in senile emphysema Some of the alveoli are dilated in this condition In the aged the alveoli become flabby like the skin The consequent dilatation of the alveoli is the result of atrophic changes in the alveolar septums corresponding to the age of the individual Similar degenerative changes prevail in all of the senescent body tissues Simultaneously some of the elasticity of the lung is lost But it is to be kept in mind that this loss is proportionate to the loss of the tone and strength of the respiratory muscles of the chest Consequently the normal functional balance remains undisturbed between the centripetal (hilusward) traction of the pulmonary elastic fibers and the centrifugal traction of the intrapleural negative pressure The latter is actuated by the outward pull of the inspiratory muscles of the chest wall In senile emphysema the respiratory excursions of the chest are reduced also because in the aged there are calcification of the costochondral junction limitation in motion of the costovertebral joints fibrosis and loss of elasticity of the thoracic ligaments loss of elasticity of the bronchi due to calcification of their walls possible pulmonary arteriosclerosis and concurrent heart failure Pulmonary congestion associated with heart failure causes a decrease in the expansibility of the lung

The Kountz Alexander type of emphysema according to the original definition of these clinicians is not primarily a pulmonary disease Changes in the lung are secondary to

TABLE I

DIFFERENTIAL DIAGNOSIS

	Pseudohypertrophic Emphysema	Senile Emphysema
Size of the Chest	Increased	Not Increased*
Shape of the Chest	Barrel like or box like	Small, flat*
Position of ribs	Horizontal	Oblique*
Position of sternum	Elevated	Not elevated*
Intercostal spaces	Widened	Narrowed*
Dorsal spine	Kyphosis	Straight or convex
Neck	Short	Normal*
Shoulders	Thrown forward	Normal*
Accessory respiratory muscles	Visible function	No hyperfunction
Epigastric angle	Widened	Normal or narrowed
Motion of epigastrium	Not protruding *on inspir*	Inspir protrusion
Pulsation of epigastrium	Present	Absent
Motion of lower ribs	Inward on inspiration	Normal
Diaphragm position	Low	Normal
Diaphragm excursions	Decreased or absent	Normal
Type of respiration	Thoracic	Abdominal
Cyanosis	Present	Infrequent or absent
X ray Costophrenic sinus	Shallow	Normal*
X ray Translucency	Increased	Normal or slight incr
X ray Lung behind sternum	Increased	Not increased*
X ray Vascular markings	Indistinct	Normal or increased
X-ray Shape of sternum	Anterior convexity	Normal
X ray A P diameter of chest	Increased	Not increased*
Pulmonary function	Insufficiency	Normal
Arterial oxygen saturation	Low	Normal
Arterial CO_2 tension	High	Normal
Signs of right heart failure	Often present	Absent
Venous pressure	Increased	Normal

* Except in the Kountz Alexander type of emphysema

an increase in the size of the thoracic cage One of the characteristic features of this condition is straightening and stiffness of the thoracic spine These changes are brought about by degenerative alterations in the intervertebral disks The nucleus or the entire disk becomes swollen In the advanced degenerative phases some of the intervertebral disks become completely separated from the bone and undergo complete dissolution With the progression of degenerative changes, the corresponding vertebral bodies become implicated, they thin out and finally, kyphosis may result This, in turn, will lead to an outward flare of the ribs and to the development of barrel chest The lung passively follows the distention of the thorax and thus it becomes somewhat enlarged in volume

Distinctive differential diagnostic aspects of pseudohypertrophic emphysema and senile emphysema are outlined in Table I

Speaking of differential diagnosis, mention should be made of "focal emphysema" described in recent years by Gough Fletcher, Hugh Jones and Heppleston Its salient characteristics are (1) deposition of "inert" dust particles in the lung, such as carbon (in coal miners), iron oxide, tin oxide, cadmium dioxide (in metal workers and miners) (2) distention of the alveoli adjacent to these deposits of foreign dust particles and also, atrophy of peribronchiolar muscles followed by dilatation of the respective respiratory bronchioles It is well to keep in mind that formerly the term focal emphysema was applied to localized areas of alveolar dilatation caused by contraction of fibrous tissue in association with healing of infections

The importance of differentiating regional emphysema secondary to partial (check valve) occlusion of one of the major bronchi, from genuine emphysema needs no special emphasis This type of obliteration of some of the lower air passageways may result from aspirated foreign body, intrinsic or extrinsic neoplasms or from compression by pathologic changes in adjacent structures

Undue pressure of oxygen given for resuscitation of the newborn may cause extensive destruction of alveoli that is, traumatic emphysema

Emphysema of both lungs may be the sequel of partial tracheal obstruction

Currently a new clinical entity has been described under the name of localized pulmonary hypertrophic emphysema (also called *congenital lobar emphysema* or regional obstructive emphysema) Emphysematous changes are segmental or lobar in extent They are localized in one of the upper lobes The exact etiology of localized hypertrophic emphysema is not known Its origin has been attributed to bronchial chondromalacia with consequent flaccidity of the bronchial wall In some instances it was assumed that bronchial occlusion resulted from mucosal folds or from compression by adjacent enlarged blood vessels

The time necessary for the development of pseudohypertrophic emphysema varies from 2 to 20 years It is predicated upon the intensity and duration of causative influences and foregone pathologic alterations in the lung tissue

Should attention be focused on the high incidence of this condition a much larger number of cases would be found than heretofore on routine chest examination in the office of the physician at the time of admission to general hospitals or at the time of mass x ray surveys Moreover such an endeavor would reveal unsuspected instances of *subclinical* emphysema Needless to say salutary therapeutic and prophylactic measures applied at this stage would bring about immeasurable benefits

The incidence of pseudohypertrophic emphysema is much higher in men than in women Occupational hazards alone without underlying disease of industrial origin have no bearing on this discrepancy The following explanation seems to be plausible In women the configuration of the chest is typically feminine with a comparatively pronounced convexity of the upper one third of the anterior thoracic wall In women the thoracic type of respiration is observed in contrast to the abdominal type of breathing seen in men The latter is a manifestation of the dominantly diaphragmatic respiration Looking at this situation from the teleological standpoint it may be said that the female chest is constituted so as to protect the undisturbed development of the pregnant uterus and to avoid constant cyclic pressure of the diaphragm descending with each inspiration upon the growing fetus Because of these anatomical and physiological peculiarities specific pathological changes of emhysema are less likely to result in clinical symptoms in women than in men

In daily practice gradations of emphysema such as slight moderate and severe are recognized Such classification may be based on the patient s complaints including the degree of work ability symptoms and signs as noted by the physician physical findings (pulmonary cardiologic and general) x ray findings cardiorespiratory function studies and biochemical data

According to Motley and his associates slight emphysema exists when the pulmonary residual air is between 25 and 35% of the total lung volume Moderate degree of emphysema is present when the ratio is between 35 and 45% With corresponding figures between 45 and 55% emphysema is advanced When residual air is more than 55% of the total lung volume emphysema is far advanced

Harvey and his associates divided their patients with emphysema into two groups (1) The diagnosis was mild emphysema when arterial oxygen saturation was normal (94–98%) or there was only a slight unsaturation at rest (90–93%) and the oxygen saturation did not decrease after exercise None of these patients showed evidence of circulatory disturbance or failure at rest (2) Severe emphysema was diagnosed when there were oxygen unsaturation of the arterial blood at rest and pronounced unsaturation after exercise

Cyclic variations in the severity of emphysema may be observed from time to time These are attributable to the following (1) Presence or absence of pulmonary infection and possible fluctuations in the intensity of the latter (2) allergic manifestations in the lower respiratory tract (3) variations in the degree of pulmonary congestion secondary to heart failure (4) reflex bronchospasm of pulmonary or extrapulmonary (somatic or psychogenic) origin

Relative to the pathogenesis of pseudohypertrophic emphysema I am of the opinion that the following factors are of cardinal importance (1) Increased intrapulmonary pressure during strenuous coughing (pulmonary pneumatic hypertension and aerodynamic trauma) (2) Infections and other pathological changes which result in extensive degenerative alterations in the supportive framework of the lung, particularly in the elastic fibers which surround the alveoli and the lower air passages (3) Bronchial disease with mucosal swelling, fibrosis or accumulation of exudate which result in a partial bronchial occlusion of the check-valve type (4) Bronchospasm

Cough is such a common symptom that more often than not it is disregarded and neglected by the individual Its constant prevalence leads to habituation to cough by the patient, by the public and by the physician The degree of pulmonary pneumatic hypertension during cough depends upon the force exerted by the expiratory muscles and upon the integrity of other pertinent components of the respiratory tract and the ventilatory mechanism Cough as a reflex mechanism is a useful defense reaction of the body, nevertheless, even under the best of circumstances it represents undue stretch and strain upon the alveoli and the elastic elements of the lung When this aerodynamic trauma is intense frequent and protracted enough, its detrimental effect is inevitable The deleterious influence of pneumatic alveolar hypertension which prevails in the lung during the compressive phase of cough can be more readily appreciated if the following changes are borne in mind (1) Air currents are subject to the same physical laws as water currents They move from a site of higher pressure toward areas of lower pressure While during quiet respiration the intra-alveolar pressure cannot be higher than the atmospheric pressure which prevails in the bronchi, during the compressive phase of strenuous coughing the intra alveolar pressure may rise to 200 mm of mercury over and above atmospheric pressure (2) The physical law of communicating vessels applies to the relationship between respiratory bronchioles and their respective cluster of alveoli The same pressure which exists in the narrow respiratory bronchiole is transmitted undiminished to the entire perimetry of all of the respective alveoli Thoracoscopic studies reveal that subpleural blebs expand on forced expiration Peyser and his collaborators demon

gen (stenosis of the lower air passages by inflammatory reaction, edema, fibrosis or spasm of the bronchial wall, angiospasm, vascular sclerosis or alveolar-capillary block), the distended alveoli are more vulnerable to tussive trauma than normal alveoli (3) In the presence of bronchial constriction the effect of traumatizing pneumatic hypertension is cumulative With each coughing spell an increment of positive pressure is added to that of air entrapped in the corresponding alveoli The resulting sustained, excessive intra alveolar hypertension culminates in rupture of the alveolar septa (4) At the termination of the compressive phase of cough, when there is a precipitous drop in the intrapulmonary pressure, evacuation of air is slower from alveoli attached to spastic, partially occluded bronchi than from alveoli connected to bronchi of normal lumen This exerts an appreciable distending influence upon the alveoli implicated This phenomenon may be referred to as regional expiratory lag It is my opinion that the existence of stenotic areas in some of the smaller bronchi explains the seemingly haphazard and bizarre topography of pulmonary bullae and blebs under the pleura The frequent localization of bullae in the upper lobe is attributable to the fact that during expiration the outrushing air from the middle and lower lobes creates resistance against the outflow of air through the upper lobe bronchus The diameter of the latter is smaller than the combined diameter of the middle and lower lobes

Destruction of a great many of the alveoli and much of the elastic elements of the lung inexorably follows chronic, severe, uncontrolled cough The harmful influence of cough upon these structures depends not only upon the severity of cough but also upon the pathologic conditions which are the incentive causes of cough and also upon the age of

the patient When as a consequence of infection the vitality of the lung tissue is impaired or because of diminished blood flow through fibrosed vessels the nutrition of these tissues is below par they become more vulnerable to the destructive force of tussive aerodynamic trauma In general tensile strength and resilience of the tissues are less in senescence than in young individuals The more advanced the age the greater the possibility of damage by pulmonary pneumatic hypertension

In reference to chronic lung infection and protracted cough undoubtedly the origin of so-called hypertrophic emphysema ordinarily encountered in older persons is traceable to early years of life in a great many instances Chronic infectious diseases of childhood with *associated pulmonary fibrosis and possible* bronchiectasis are potent agents in initiating pathologic sequels the ultimate result of which is emphysema Long standing allergic bronchial asthma may have an identical influence Oftentimes infections of this type heal after a prolonged course Patients with emphysema who seek medical attention may completely forget about them But there remain destructive alterations in the lung tissue It may seem paradoxical that in the presence of such lung changes no manifest emphysema is evident during the early years of life The reason for the absence of symptoms of emphysema in these young persons is that the elastic fibers of the lung which remained intact continue to function with a capacity sufficient to maintain the normal respiratory motions of the lung Subjective and objective manifestations of emphysema become obvious however when these individuals reach old age At this time the previously *intact elastic* fibers either undergo senile degeneration or are damaged by intercurrent lung infections or by bouts of severe coughing

Spasm is one of the basic homeostatic mechanisms of the body Widespread bronchospasm is more common occurrence than *generally realized Its presence* in allergic bronchial asthma is well known It is less well known that *emphysema* is the most frequent *complication* of bronchial asthma Spasm of the peribronchial and peribronchiolar smooth muscles may be provoked by *infections of the* lower respiratory tract, by *inflammatory hyper*emia or congestion in the bronchial mucosa due to failure of the left ventricle and by extensive pulmonary *fibrosis In addition to in*fection and exposure to cold mention should be made of smoking as a common cause of bronchitis bronchiolitis and bronchospasm There is a definite association between smoking and emphysema Excessive cortical and hypothalamic stimuli are readily transmitted *to the nerve center of the vagus Pronounced* stimulation of the latter may initiate *efferent* impulses with consequent production of acetylcholine at its peripheral nerve endings This in turn may culminate in bronchospasm Apropos of vagal stimulation it is worthwhile to cite the observations of Greene *and Dundee In 700 consecutive necropsies* in males they found peptic ulcer in 6.4% in persons without emphysema and in 19% (three times higher incidence) in persons with emphysema Lowell and his associates noted peptic ulcer in 24% of patients with emphysema Also close association between these two conditions was recorded by *Weber and Gregg*

Bronchospasm particularly in the presence of congestion and edema of the bronchial mucosa may produce a check valve stenosis The latter permits the ingress of air to distal portions of the lung but prevents its egress *In this manner the trapping of some of the* air inhaled results in a retrograde stretching and tearing of the alveoli and their elastic components

Emphysema begets emphysema The distended alveoli in a state of pneumatic hypertension exert pressure upon adjacent intact alveoli capillaries and blood vessels Compression of the nutritional vessels of normal alveoli is bound to lead to atrophy and consequent structural weakening of the air cells and respective air passages Also the lengthened tortuous *respiratory bronchioles* may be compressed so as to set up a check valve mechanism within their lumen Consequent intra alveolar trapping of air is most pronounced during coughing Proneness to this event is obvious when one *thinks of the loss* of bronchiolar patency secondary to loss of

elasticity The latter is the medium which transmits the outward traction of the intrapleural negative pressure

There is a prevalent mistaken notion concerning the distended state of the thoracic cage in emphysema Erroneously it is attributed to dilatation of the emphysematous lung This however is not the case Actually distention of the thorax as well as the enlargement of the lung are brought about by the same factor namely the loss of the elastic contractility of the lung

The lung is kept in its physiologically stretched out position by two forces (1) the pressure of the atmospheric air (2) the centrifugal suction effect of the intrapleural negative pressure The thoracic cage is larger than the lung Even so the lung is held in apposition to the inner surface of the chest wall by the traction of the intrapleural negative pressure The latter is an expression of the difference between the pressure of the atmospheric air reaching the lung through the lower air passages and the innate centripetal (hilusward) retractility of elastic elements of this organ The intrapleural pressure is less than the atmospheric pressure It is about —5 0 mm of mercury on inspiration and —1 5 mm of mercury on expiration

Decrease in or complete loss of elasticity of the lung is considered the most important pathological defect in pseudohypertrophic emphysema Empirical observations in this respect have been corroborated by precise investigative studies of Christie Fry and his associates and others When as the result of loss of the elastic elements of the lung its centripetal (hilusward) contractility is greatly decreased there is a proportionate decrease in or complete disappearance of the negativity of the intrapleural pressure In some patients it is positive The inspiratory muscles of the chest wall not being obliged to counteract the inward pull of the intrapleural negative pressure are bound to distend the thoracic cage This train of events is similar to that seen when initial artificial pneumothorax is given Measurements carried out by Bjoerkman showed that only one fifth of the air injected resulted in pulmonary relaxation while four fifths was taken up by expansion of the chest wall For completeness sake it should be added that formation of air cysts of increased pressure may contribute to the distention of the thoracic cage

The normal position of the diaphragm is the direct result of the upward traction force of the intrapleural negative pressure In emphysema in consequence of the disappearance of the upward traction of the intrapleural pressure the diaphragm occupies a constant low (inspiratory) position Clinically it is easily demonstrable that the diaphragm occupies a low position after the establishment of artificial pneumothorax Also it is known that the respiratory excursions of the diaphragm are restricted following the institution of artificial pneumothorax The reason is that in an abnormally low position the diaphragm is functionally handicapped or completely defunctionalized In emphysema its respiratory motions are slight absent or may be paradoxical rising on inspiration and descending on expiration The paradoxical motion of this muscle is attributable to the fact that when the diaphragm remains in its abnormally low position for an extended period of time it becomes atrophic The atrophic muscle having lost its autochton capacity to function is likely passively to follow the influence of the intrapleural pressure slight though it may be There are corresponding paradoxic changes in the intraperitoneal pressure The latter is higher than normal in emphysema and it shows only slight variations during the respiratory phases

The experimental studies of Garcia Ramos demonstrated that undue distention of the lung causes spasm of the diaphragm with consequent lowering of its position and interference with its function There are other factors which to a lesser extent may contribute to the low position of the diaphragm These are (1) distention of air cysts of increased pressure (2) hypoxia of diaphragmatic muscle fibers with consequent spasm pain and dysfunction (3) stretching of the diaphragm by widening of the lower part of the chest

On the basis of a composite study Wilson reported that the diaphragm contributed from 37 to 47% of the respired air ventilated on

quiet respiration With the decrease or loss of diaphragmatic function the previously abdominal type of respiration is changed into thoracic type The longer the duration of *emphysema the greater is the likelihood for* the development of atrophy of disuse of the diaphragm This possibility has an important bearing upon the therapeutic benefits of measures which aim at the restoration of the normal position of this muscle Obviously with less extensive atrophic changes in the diaphragm the chances are better for restoring its normal function Thus early treatment with this purpose in mind is axiomatic It is well to remember in this connection that the functional capacity *of the diaphragm is decreased* in the aged because its central tendon becomes more fibrous and constitutes a greater *part of this structure than in the young*

Ventilatory incompetence of the lung in emphysema is aggravated by the distention of the chest wall Inspiratory muscles attached to the chest wall are unable to cause further dilatation of the thoracic cage or at the most their function in this respect is far below par Consequently the accessory inspiratory muscles come into play (sternomastoid scaleni and pectoralis minor) This is easily noticeable in a great many instances of emphysema In the aged there is a decreased tonicity of the respiratory muscles like in all of the striated muscles of the body This represents *an added handicap as far as ventilatory competence* of the lung is concerned

Pulmonary insufficiency resulting from the derangement of diaphragmatic *function and* diminished capacity of the muscles of the chest wall is associated with a faulty distribution of the inhaled air As shown by the investigations of Nielsen and Sonne Sonne Roelsen Darling Cournand and Richards the distribution of inhaled air is uneven in normal lungs It was pointed out by Christie that in addition to the destruction of the alveolar capillary gear there are two other factors responsible for the impairment of aeration (1) By dilatation of the alveolar ducts their jet like effect upon the inspired air *is largely* lost Consequently remote alveoli belonging *to these ducts are inadequately* ventilated (2) With the loss of pulmonary elasticity the ventilation of the emphysematous lung is uneven *Deeper lying alveoli* which are anatomically intact and which are provided with *normal capillary blood supply* are receiving only a small portion of the air current If the intrapleural pressure were negative in emphysema the tidal air would move into alveoli with elastic fibers which are receiving traction from the pleural space But in emphysema there is slight or no intrapleural suction so there is no traction upon intact elastic alveoli Consequently the tidal air finds its way to large flabby inelastic emphysematous alveoli As a matter of fact elastic fibers of intact alveoli—in the absence *of pleural suction—represent resistance against* the inflow of air The inadequate ventilation of emphysematous areas may readily be appreciated *when one thinks of the relatively* small caliber of bronchioles leading to them Even forced expiration does not remove more than one third of the air from the alveoli This stagnation of air is associated with tussive insufficiency It is known that in coughing compression of the air inhaled is the expulsive force which actuates its sudden outflow from the lower air passages when the glottis opens In emphysema the compressive phase of cough is ineffective also because of loss of pulmonary recoil In the absence of effective compression of the tidal air there is no gradient for the air to flow from the lung to the pharynx during the expulsive phase of cough This maldistribution and inadequate air flow in the lung of emphysematous patients *may aptly be designated* as pulmonary pneumatic dyskinesia

Hemorespiratory insufficiency of emphysematous patients results in rapid and shallow respirations on exertion and in severe cases even at rest Inspirations are irregular Expiration is prolonged strenuous and incomplete A crude but impressive illustration of this point is the inability of the emphysematous patient to blow out the lighted candle

In instances where there is an associated *failure of the left ventricle* the concomitant pulmonary congestion causes diminished distensibility of the lung This of course represents added respiratory handicap

Function studies reveal characteristic combination of findings

(1) Tidal air is normal or slightly reduced

(2) The complemental air is reduced

(3) The functional residual air is from two to three times that of normal

(4) The maximum breathing capacity is reduced The reduction may be as much as 50% or more

(5) The vital capacity of the lung may be lowered by from 20 to 60% In some instances the vital capacity of the lung remains normal

(6) The volume of air exhaled during the first the first 2 and first 3 seconds of forced expiration is greatly diminished in patients with genuine emphysema as compared with normal persons In the latter according to Gaensler the respective per cent of the vital capacity are 83 94 and 97 In patients with emphysema he recorded the following figures 42 57 and 68% on the vital capacity of the lung

(7) Carbon dioxide content of the alveoli is increased to 7 to 8% (50–60 mm) of mercury Retention of excess of carbon dioxide leads to respiratory acidosis The carbon dioxide content of arterial blood fluctuates parallel to alveolar carbon dioxide levels All patients with genuine emphysema have some degree of carbon dioxide intoxication

(8) Oxygen saturation of the blood is below normal It may be as low as 60%

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(10) Plasma chlorides are decreased

(11) Venous pressure is elevated

(12) There is pulmonary hypertension

(13) Polycythemia is present without pathologic bone marrow changes

(14) The size of the erythrocytes is increased Wilson and his associates found a 14% increase in the mean corpuscle volume in patients with pseudohypertrophic emphysema

(15) Donald and Christie noted that following the inhalation of 4% carbon dioxide for a period of five minutes the respiratory response is impaired in patients with genuine emphysema Also Scott Meakins and Davis observed lack of respiratory response to carbon dioxide in these patients

As a commentary it may be said that it is well to use the various pulmonary function tests in combination rather than to rely on a single procedure Pulmonary hypertension in emphysema is attributable to increased vascular resistance in the lung which is brought about by the following causes (1) destruction and compression of capillaries and precapillary arterioles (2) pulmonary vasospasm due to hypoxia (3) pulmonary vasospasm due to hypercapnia (4) possible sclerosis of the pulmonary arterioles Borden and his co workers found no close correlation between the degree of pulmonary hypertension and the severity of emphysema estimated on the basis of altered ratio of residual air to total lung volume

Dyspnea is the most conspicuous symptom of genuine emphysema It is greatly influenced by the oxygen requirement of the patient at any given time It may be entirely absent during rest while in some instances administration of oxygen may be necessary to keep the patient comfortable even in bed As a rule subjectively and objectively noticeable dyspnea is provoked by various degrees of physical effort such as climbing stairs walking short distances or doing manual labor Symptoms associated with hypoxia and hypercapnia include headache giddiness insomnia tremor fatigue weakness and nausea Wheezing is a common symptom It is brought about by the presence of inflammatory exudate in the lower air passages and by bronchospasm Frequency and severity of cough are dependent upon the type and extent of coexistent bronchitis pulmonary fibrosis bronchospasm other pathologic changes in the lung and also upon the competence of the heart in maintaining adequate pulmonary circulation Sometimes the patient complains of expectoration of scanty viscid mucoid sputum The latter may be purulent or blood streaked in bronchitis Frank hemorrhage from the lung is uncommon Occasionally tightness in the chest is complained of Abdominal pain particularly in the epigastric region may result from cardiac decompensation with swelling of the liver Some of the lower chest pain is

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due to spasm of the diaphragm in its abnormally low position and hypoxia of this muscle as well as of the intercostal muscles

Taking a thorough history is helpful in arriving at the correct diagnosis One should inquire about foregone serious acute or protracted *diseases of the lung* and about long standing cough Influenza unresolved pneumonia chronic bronchitis tuberculosis sarcoidosis pneumoconiosis fungus infection and allergic asthma are of importance in this regard In addition to harmful dusts likely to cause pneumonoconiosis particular attention should be paid to prolonged exposure to noxious fumes and gases

On physical examination cyanosis and dyspnea may be obvious Dyspnea may appear less pronounced than cyanosis for the reason that because of the protracted increase in the carbon dioxide content of the blood the respiratory center becomes less sensitive to this gas as a stimulant In the sitting position the patient may rest his arms on his knees so as to assure more effective function of the accessory inspiratory muscles The rapid strenuous contractions of the latter are easily noticeable It is well to observe the epigastrium *Cyclic protrusions* of the epigastrium on inspiration are absent or decreased In *some patients* paradoxic motions are noted in this region corresponding to the respiratory *phases* Patients suspected of having emphysema should be examined in the upright position except when general debility *obviates it so as to prevent elevation of the* diaphragm by the pressure of the abdominal viscera

In some instances one may observe "purse *lip" expiration* The patient exhales with his mouth closed except a narrow opening as if whistling In this manner the intrapulmonary pressure increases and the tidal air is forced to wider areas of the lung This permits *better oxygenation* of the blood in the lesser circulation

The so called barrel chest is one of the characteristic manifestations of pseudohypertrophic emphysema Kyphosis of the spine affects the entire thoracic region *The ribs* are widely separated and occupy a horizontal instead *of the normal* slanted position Distention of the large cervical veins signifies decrease in the negativity of the intrathoracic pressure which interferes with the flow of blood toward the right auricle The larynx appears in a position lower than normal This should not be interpreted as ptosis of the larynx rather it is attributable to the elevation of the anterior aspect of the thoracic cage

Hyperresonance is observed on percussion over both lungs One can ascertain limited respiratory excursions of the diaphragm on physical examination Also one is likely to find reduction in the size of the cardiac dullness and liver dullness

Breath sounds are diminished Expiration is prolonged labored and inadequate This can be graphically shown on kymographic tracings taken with a recording spirometer A standard basal metabolism apparatus can be used for this purpose In this manner it is possible to demonstrate that a patient with pronounced emphysema is unable to deflate his lung When a standard spirometer is used for determining the vital capacity of the lung it takes from three to five times longer to fill the metal cylinder for an *emphysematous* patient than for a normal individual

On auscultation one often finds sonorous and sibilant rales over the entire extent of both lungs

As in a number of other pulmonary *diseases* associated with destruction of the lung parenchyma clubbing of the *fingers may* be observed in emphysema

With failure of the right ventricle one finds an enlarged palpable liver and edema of the *ankles and lower extremities*

Examination of the eye grounds may reveal papilledema Cameron in 1933 first reported this finding in emphysema According to Simpson its cause is not increased *venous pressure or polycythemia He expressed the* view that lack of oxygen in and increase of the carbon dioxide content of the blood were responsible for cerebral vasodilatation and papilledema

Venous pressure is increased in *emphysema* because the lessened negativity *of the intrathoracic pressure hampers the return* flow of blood from the periphery of the greater circulation to the heart May found that en

largement of the veins of the undersurface of the tongue when an individual is sitting or standing is a reliable sign of increased venous pressure

Roentgenologic examination of the patient should include postero anterior and lateral roentgenograms of the chest and fluoroscopic study In a typical case the following findings are noted

(1) The lung fields are enlarged

(2) There is kyphosis of the entire thoracic spine

(3) The ribs occupy a horizontal position

(4) The intercostal spaces are widened

(5) The anterior and posterior mediastinal spaces are enlarged

(6) The lung fields show increased x ray translucency

(7) The costophrenic sinuses are wider than normal

(8) The diaphragm occupies a low position and its upward convexity is decreased or entirely lost

(9) The respiratory excursions of the diaphragm are slow decreased absent or paradoxical

(10) The heart shadow is small in the absence of cardiac hypertrophy or dilatation One should keep in mind that the heart may seem comparatively small because of the pronounced enlargement of the lung fields the low position of the diaphragm and the clockwise rotation of the heart Decrease in the size of the heart shadow however is partly real The actual decrease in the size of the heart is attributable to the lessened negativity of the intrathoracic pressure This in turn means decreased flow of blood to the heart through the superior and inferior venae cavae

(11) Changes responsible for the so-called anemic lung in emphysema were beautifully demonstrated by Robb and Steinberg by means of pulmonary angiography (intravenous injection of 70% diodrast) They describe the diminished vascularity of the lung as follows The main branches of the pulmonary artery at the hili and in the lower lobes were enlarged forming a so called moustache while in the midzone and outer zones the vessels become small and wirelike"

(12) Roentgenograms taken after bronchograms reveal a narrowing of the bronchial tubes

While these roentgenologic findings are valuable in establishing the diagnosis one should keep in mind that normal roentgenograms of the chest do not rule out the diagnosis of hypertrophic emphysema Christie reported that out of 11 emphysema cases confirmed by postmortem examination the roentgenogram was suggestive of this disease only in 5 or 45%

TREATMENT

There is no justification for therapeutic defeatism concerning the management of pseudo hypertrophic emphysema A number of drugs and methods are available which may bring about satisfactory symptomatic relief and thus help in the rehabilitation of the disabled patient

(1) I teach all of my patients expiration with pursed lips They get readily used to it and appreciate its simplicity and value in bringing about a degree of relief from dyspnea Its use as a purposeful therapeutic measure was first advocated by Schutz in 1935

(2) Manual compression of the lower anterior parts of the chest the upper part of the abdomen or both rhythmically at intervals corresponding to the expiratory phase of the respiratory cycle has been found to be helpful by clinicians in this country and abroad during the past few decades

(3) Good therapeutic results have been reported from the use of especially constructed abdominal supports first recommended by Gordon (1934) and Kountz and Alexander (1934) Gordon says "A suitable abdominal support consists of a pad two cross springs a back piece and straps for adjusting the degree of pressure The effects are attributed to the increased abdominal pressure obtained by the through and through action of the pad and cross spring assembly

(4) Breathing exercises aim at establishin

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The so called barrel chest is one of the characteristic manifestations of pseudohypertrophic emphysema Kyphosis of the spine affects the entire thoracic region The ribs are widely separated and occupy a horizontal instead of the normal slanted position Distention of the large cervical veins signifies decrease in the negativity of the intrathoracic pressure which interferes with the flow of blood toward the right auricle The larynx appears in a position lower than normal This should not be interpreted as ptosis of the larynx rather it is attributable to the elevation of the anterior aspect of the thoracic cage

Hyperresonance is observed on percussion over both lungs One can ascertain limited respiratory excursions of the diaphragm on physical examination Also, one is likely to find reduction in the size of the cardiac dullness and liver dullness

Breath sounds are diminished Expiration is prolonged labored and inadequate This can be graphically shown on kymographic tracings taken with a recording spirometer A standard basal metabolism apparatus can be used for this purpose In this manner it is possible to demonstrate that a patient with pronounced emphysema is unable to deflate his lung When a standard spirometer is used for determining the vital capacity of the lung it takes from three to five times longer to fill the metal cylinder for an emphysematous patient than for a normal individual

On auscultation one often finds sonorous and sibilant rales over the entire extent of both lungs

As in a number of other pulmonary diseases associated with destruction of the lung parenchyma clubbing of the fingers may be observed in emphysema

With failure of the right ventricle one finds an enlarged palpable liver and edema of the ankles and lower extremities

Examination of the eye grounds may reveal papilledema Cameron in 1933 first reported this finding in emphysema According to Simpson its cause is not increased venous pressure or polycythemia He expressed the view that lack of oxygen in and increase of the carbon dioxide content of the blood were responsible for cerebral vasodilatation and papilledema

Venous pressure is increased in emphysema because the lessened negativity of the intrathoracic pressure hampers the return flow of blood from the periphery of the greater circulation to the heart May found that en

largement of the veins of the undersurface of the tongue when an individual is sitting or standing is a reliable sign of increased venous pressure

Roentgenologic examination of the patient should include postero anterior and lateral roentgenograms of the chest and fluoroscopic study In a typical case the following findings are noted

(1) The lung fields are enlarged

(2) There is kyphosis of the entire thoracic spine

(3) The ribs occupy a horizontal position

(4) The intercostal spaces are widened

(5) The anterior and posterior mediastinal spaces are enlarged

(6) The lung fields show increased x ray translucency

(7) The costophrenic sinuses are wider than normal

(8) The diaphragm occupies a low position and its upward convexity is decreased or entirely lost

(9) The respiratory excursions of the diaphragm are slow decreased absent or paradoxical

(10) The heart shadow is small in the absence of cardiac hypertrophy or dilatation One should keep in mind that the heart may seem comparatively small because of the pronounced enlargement of the lung fields the low position of the diaphragm and the clockwise rotation of the heart Decrease in the size of the heart shadow however, is partly real The actual decrease in the size of the heart is attributable to the lessened negativity of the intrathoracic pressure This in turn means decreased flow of blood to the heart through the superior and inferior venae cavae

(11) Changes responsible for the so called anemic lung in emphysema were beautifully demonstrated by Robb and Steinberg by means of pulmonary angiography (intravenous injection of 70% diodrast) They describe the diminished vascularity of the lung as follows "The main branches of the pulmonary artery at the hili and in the lower lobes were enlarged forming a so called moustache while in the midzone and outer zones the vessels become small and wirelike"

(12) Roentgenograms taken after bronchograms reveal a narrowing of the bronchial tubes

While these roentgenologic findings are valuable in establishing the diagnosis one should keep in mind that normal roentgenograms of the chest do not rule out the diagnosis of hypertrophic emphysema Christie reported that out of 11 emphysema cases confirmed by postmortem examination the roentgenogram was suggestive of this disease only in 5 or 45%

TREATMENT

There is no justification for therapeutic defeatism concerning the management of pseudo hypertrophic emphysema A number of drugs and methods are available which may bring about satisfactory symptomatic relief and thus help in the rehabilitation of the disabled patient

(1) I teach all of my patients expiration with pursed lips They get readily used to it and appreciate its simplicity and value in bringing about a degree of relief from dyspnea Its use as a purposeful therapeutic measure was first advocated by Schutz in 1935

(2) Manual compression of the lower anterior parts of the chest the upper part of the abdomen or both rhythmically at intervals corresponding to the expiratory phase of the respiratory cycle has been found to be helpful by clinicians in this country and abroad during the past few decades

(3) Good therapeutic results have been reported from the use of especially constructed abdominal supports first recommended by Gordon (1934) and Kountz and Alexander (1934) Gordon says "A suitable abdominal support consists of a pad two cross springs a back piece and straps for adjusting the degree of pressure The effects are attributed to the increased abdominal pressure obtained by the through and through action of the pad and cross spring assembly"

(4) Breathing exercises aim at establishing

a habit of forced expiration with the volitional contraction of the large expiratory muscles of the abdomen (rectus, external and internal oblique and transversus). In this fashion the induced elevation of the diaphragm facilitates emptying the lung of tidal air. This, in turn, is followed by a more competent inspiration.

(5) *Surprising relief of dyspnea* may be experienced by patients who train themselves in lying in a slanted head down position. The foot of the bed is elevated 18 inches. The abdominal viscera force the diaphragm to a high position. It has been demonstrated experimentally as well as clinically that in this manner diaphragmatic excursions are increased and the functional residual lung volume is greatly reduced and consequently, the ventilatory competence of the lung is substantially enhanced.

(6) Artificial pneumoperitoneum is a logical measure for the treatment of pseudohypertrophic emphysema. Technically it is a safe and simple procedure that can be carried out by a physician of average manual dexterity. *Technical details are given in the author's* previous publications.

Artificial pneumoperitoneum elevates the diaphragm and thereby refunctionalizes this *previously defuntionalized muscle*. The resulting improved respiratory excursions are comparable to restoration of function after reduction of a dislocated joint. Normal diaphragmatic movements are predicated upon a gradient which exists between the thoracic cage with its negative pressure and the abdominal cavity with its predominantly atmospheric pressure. Artificial pneumoperitoneum is instrumental in establishing such a gradient by its positive pressure, contrasted to the *nearly atmospheric pressure* in the pleural space encountered in pronounced emphysema.

Pneumoperitoneum may decompress some of the large air cysts and thus decrease their interference with the ventilatory and respiratory function of intact alveoli and capillaries. Also, elevation of the diaphragm reduces the size of the lung. Consequently, the amount *of residual air, which dilutes* and vitiates the tidal air, is diminished.

Under the influence of artificial pneumoperitoneum, the *intrapleural pressure* becomes more negative. This greater negativity draws the diaphragm *upward and the chest* wall inward. In consequence of the latter, the inspiratory muscles of the chest wall are likely to regain some of their *normal function* and thus increase respiratory excursions of the chest wall.

With the improved function of the respiratory muscles, *including the diaphragm, a more* even and widespread distribution of the inhaled air is made possible. Better oxygenation of the blood is brought about.

Improved respiratory function of the thorax together with the increased negativity of the intrapleural pressure facilitate the venous return from the periphery of the greater circulation to the heart and the flow of blood from the right ventricle to the lung.

(7) Experience has convinced me that it is advantageous to administer bronchospasmolytic drugs capable of relieving concomitant spasm of the peribronchial and peribronchiolar smooth muscles. Epinephrin in 1:100 solution is given in the form of aerosolized inhalations. *Also, good results can be expected from* inhalation of aerosols of Vaponephrine which is a 2.25% solution of racemic epinephrine hydrochloride. Another excellent relaxant of bronchospasm is isopropylepinephrine (available under the *proprietary name* of Isuprel, Aludrine, Norisodrine, Isonorm and I.P.A.). I prefer to administer isopropylepinephrine in the form of sublingual tablets of 10 mg. every 3 to 4 hours. Also it may be given as an aerosol of a solution of 1:200. *Cartridges of* micropulverized powder of this drug are available for use with a special inhaler. It has been reported that the combination *of iso-*

Neosynephrine hydrochloride, a compound *closely related to epinephrine* is given as an aerosol in a 1:100 solution. The dose of ephedrine varies from 3/8 gr. to 1 gr. and *it is given* with 1/4 gr. *of Amytal or 1/2 gr. of pheno*barbital. Orthoxine is an ephedrine like synthetic drug. It is available *in the form of* tablets of 100 mg. and as a syrup, each *tea*spoonful of which contains 50 mg. of the drug.

Propadrine another closely related preparation is given in the form of capsules containing $^3/_8$ gr or $^3/_4$ gr of the drug Theophylline with ethylenediamine is a remarkably effective bronchorelaxant It may be given rectally by inhalation or orally The newer corticosteroids prednisone and prednisolone are potent bronchospasmolytic drugs Initially 15 mg are given daily in divided doses As soon as expedient, the patient should be kept on a maintenance dose of 2.5 to 5 mg a day Because of possible side reactions the patient is kept under close observation These drugs are not to be given to individuals with diabetes hypertension congestive heart failure or peptic ulcer My results with anticholinergic preparations (parasympathetic blocking agents) have been highly satisfactory I prefer the administration of Antrenyl bromide (diethylmethyl ammonium bromide) Other clinicians recorded good results with Monodral bromide Pro banthine and Benthyl hydrochloride

(8) Acetazoleamide (Diamox) is considered a useful adjunct in that it may relieve hypercapnia by renal elimination of carbon dioxide in the form of bicarbonate Acetazoleamide is an inhibitor of the enzyme carbonic anhydrase Two tablets 250 mg each are given on arising daily It has a diuretic effect

(9) In cases of distressing dyspnea oxygen is given in gradually increased concentrations starting with less than 50% through a nasal catheter High concentrations of oxygen are hazardous Hypoxia stimulates respiration through the chemoreceptors of the aortic and carotid bodies When sudden administration of high concentrations of oxygen stops these homeostatic reflexes headache weakness somnolence coma and death may result from the consequent carbon dioxide intoxication

(10) Intermittent positive pressure breathing of oxygen first introduced by Motley and his associates represents a significant advance in the management of patients with emphysema One hundred per cent oxygen is administered with the aid of a special apparatus for a 15 minute period three times a day in severe cases on the hour Bronchospasmolytic drugs detergents and antibiotics may be given with the oxygen if circumstances require

(11) Good results have been reported by Barach with the use of an apparatus inducing expiration with negative pressure This method may aid not only the ventilation of the lung but also in the evacuation of large non functioning pulmonary cysts and in the removal of inflammatory exudate from the lower air passages

(12) Electric stimulation of the diaphragm the muscles of the anterior abdominal and thoracic walls have been reported as having beneficial effect upon the respiratory function of these structures

(13) For the purpose of reducing oxygen requirements of the body and thus alleviating dyspnea thyroidectomy was suggested by Singer in 1937 With the same idea in mind Gallaher in 1955 advocated the use of radioactive iodine (I^{131}) so as to reduce thyroid function and the metabolic rate

(14) Surgical intervention may be mandatory in some instances of pseudohypertrophic emphysema Resection of a large pulmonary cyst may be of advantage so as to prevent contamination of the tidal air with the stale non oxygenated air content of these bullae Waterman points out that in patients who may not be able to withstand major thoracic surgery of this type drainage of these air spaces by the Monaldi Head Avery technique is the procedure of choice For the relief of severe bronchospasm Abbott recommends unilateral resection of the vagus distal to the recurrent laryngeal nerve section of the bronchial branches of the recurrent laryngeal nerve and transsection of vagal branches proximal to the recurrent laryngeal nerve In addition to vagectomy resection of the pulmonary plexus is claimed to bring about favorable results

(15) For the relief of rapidly increasing venous pressure in right ventricular failure secondary to emphysema venesection is indicated Administration of one of the digitalis preparations is called for in myocardial failure Diuretics may be required for the alleviation of pulmonary congestion and edema

(16) Obese patients should be put on a reducing diet so as to attain and maintain standard body weight Obesity not only de

mands larger oxygen intake but also it interferes with the cyclic respiratory excursions of the diaphragm

(17) Infections of the respiratory tract are to be treated promptly and adequately so as to minimize obstruction of the lower air passages by mucosal swelling, inflammatory exudate and secondary bronchospasm

(18) Bronchial irritation from industrial or other environmental sources should be avoided No patient with emphysema should be permitted to smoke Tobacco smoke is bound to cause laryngitis, tracheitis, bronchitis, bronchospasm, pulmonary vasoconstriction and cough, with their potential adverse sequels

(19) Emphysema is the most frequent and most serious complication of allergic bronchial asthma All patients with pseudohypertrophic emphysema should be scrutinized for the presence of underlying asthma Immediate attention to the latter is a prerequisite of proper treatment

(20) *Harmful effects of unproductive cough* have been discussed in the text Their seriousness calls for adequate control of this symptom

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CHAPTER 15

Pulmonary Edema and Congestion

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The lungs are extremely susceptible to circulatory disorders Indeed much of the work of the cardiologist is directed toward relief of symptoms produced in the lungs by congestive heart failure It is a common problem of the physician to attempt to distinguish between symptoms caused by some primary pulmonary disease and those resulting from a cardiac condition This distinction is of critical importance because the therapeutic approach will be quite different in the two cases Not infrequently pulmonary inflammation perhaps only a mild infectious bronchitis may disturb the circulatory equilibrium in the lungs of an elderly person sufficiently to lead insensibly from an inflammatory pulmonary disease into congestive heart failure This is confusing to the physician for he may be led to the false belief that the infection is continuing despite his efforts when appropriate treatment would be cardiac therapy Even the most careful examinations utilizing all clinical radiologic electrocardiologic and laboratory methods may fail to make the distinction between cardiac and pulmonary symptoms (especially dyspnea)—the final solution resulting from the therapeutic test of cardiac therapy (especially diuretics and digitalization)

PULMONARY CONGESTION

Pulmonary congestion is ordinarily a manifestation of cardiac disease and is dealt with extensively elsewhere The pulmonary aspect of the problem is but one phase of circulatory failure but often is that which produces the dominant symptoms in congestive heart failure

In addition to the chronic passive congestion of cardiac origin there is an "active hyperemia" phase to acute pulmonary inflammation especially well known in the earliest phase of severe and extensive pneumonia Not infrequently pneumococcal pneumonia has resembled cardiac disease during the first few hours of the infection

Pulmonary congestion and pulmonary edema are inseparable conditions clinically in many circumstances Radiologically pulmonary congestion is demonstrated by an increase in the caliber of pulmonary vessels an apparent increase in their number and demonstration of the vascular shadows in the outer zones of the lung fields Stereoscopic inspection of the pulmonary vascular system in well prepared roentgenograms by a skillful radiologist with special interest in pulmonary diseases will often reveal more accurately the physiologic state of the lungs and heart than can be determined by much more elaborate clinical and laboratory procedures In addition to the appearance of the vascular tree the presence of pleural effusion even in small amount and the degree of cardiac dilation and hypertrophy reveal not only diagnostic information of high reliability but serial examinations often demonstrate therapeutic effects or progression of disease which could not be so well detected otherwise Although pulmonary edema and pulmonary inflammation are not easily separable on radiologic grounds the radiologist may frequently supply the crucial information

which solves an otherwise difficult problem of distinguishing between cardiac dyspnea and pulmonary dyspnea

Cough may be a dominant symptom in pulmonary congestion and be ascribed incorrectly to primary pulmonary disease This confusion may be heightened when the radiologist—having been told of the cough—reports radiologic findings of "bronchitis" Increased bronchovascular markings are more likely to be of circulatory than of inflammatory origin Inspection of the sputum may be very helpful in such cases If it is heavily laden with pus and if it contains many bacteria in smears stained by Gram s method the factor of infection may be important, even when heart disease is present

THE CLINICAL SYNDROME OF ACUTE PULMONARY EDEMA

The clinical picture of acute pulmonary edema in a typical and advanced case is often dramatic and terrifying and when once seen *it is not likely to be forgotten The attending physician sometimes may arrive at his diagnosis* immediately on entering the room when he hears the noisy labored breathing with rhonchi and rales readily audible at a distance The prognostic import of this sound is indicated by its popular designation as the death rattle" The patient may be in coma *and making little effective effort to expectorate* the obviously great volume of liquid sputum which has a characteristic appearance The typical sputum of a patient with advanced pulmonary edema is thin watery pinkish in color and often frothy in consistency and when it is permitted to settle in a glass container it may closely resemble the blood plasma of which it is largely composed This *material may be expectorated in great volume* if the patient s general condition is such that he can make an effective effort to dispose of the sputum as it is being formed

Deep cyanosis is the characteristic color of the face and extremities of the patient suffering from advanced pulmonary edema Often the color is unusually dark and the superficial veins especially of the face neck and upper extremities are visibly distended This hue and the distended veins constitute evidence *of increased venous pressure in the systemic* circulation In some instances the peripheral circulation has failed to such a point that the extremities are dark and cold or blotchy purple

Palpation of the thorax will yield little additional information but vibrations from the loudly audible rhonchi and rales may be felt by the examining hand Circulation in the capillaries of the skin may be of such a sluggish *character that the white imprints of the examiner s hand will remain for some time* If the systemic venous pressure is markedly elevated it will be noted that the veins of the hands do not collapse even when elevated to a maximal degree

Percussion usually will reveal extensive regions of dullness due to the underlying pulmonary disease such as pneumonia which may have been the original basis for development of pulmonary edema In addition the "waterlogged lung will have lost some of its normal resonance especially in the posterior portions of the lower lobes

Auscultation with the stethoscope will further emphasize the heavy bubbling rales coarse rhonchi and similar sounds originating *especially in the larger bronchi and in the* trachea Often these sounds are of such intensity that it is scarcely possible to hear the heart sounds Coarse bronchial breathing probably will be heard especially at the bases posteriorly Although a considerable amount of pleural fluid is likely to be found subsequently by the pathologist the classical findings of pleural effusion are often not elicited on physical examination even immediately prior to death

The roentgenographic view of the thorax in a case of acute pulmonary edema may present a varied picture usually resembling that of an extensive patchy infiltration of greatest intensity at the bases and in the hilar regions it often reveals large more or less circumscribed areas of increased density which may occupy

a considerable portion of the lung fields Acute cardiac dilatation is frequently present but this often cannot be clearly recognized in the roentgenograms because they are ordinarily made with a portable apparatus at short distance with resulting distortion of the cardiac silhouette If the patient has not been required to sit upright when the roentgenographic exposure is made free pleural fluid may not be clearly evident but may be suspected when diffuse haziness is present

The differential diagnosis of acute pulmonary edema would involve consideration of any other pulmonary disease with equally abundant sputum of any character which might produce similar auscultatory findings and in a similar manner serve as a mechanical obstruction to normal respiration The most frequently encountered condition which resembles acute pulmonary edema is extensive pneumonia with a large volume of thin purulent sputum which floods the tracheobronchial tree This picture is occasionally seen after extensive postoperative pulmonary infection of aspirational type particularly if the infection has progressed to the point of producing multiple small abscesses In many of these instances pulmonary edema also may develop during the terminal stages of the disease Any other suppurative pulmonary disease which produces an adequate volume of sputum could be confused with acute pulmonary edema if the entire background of the illness were not taken into consideration The visual inspection of the sputum is of great value and in all instances effort should be made to secure sputum for gross examination If the sputum is found to be of markedly purulent character it is probable that an inflammatory process is the outstanding one rather than the factor of altered pulmonary circulation It may be a matter of considerable importance to gain an impression as to whether the disturbance is primarily an inflammatory one or a circulatory one because the therapeutic approach may differ in the two instances Since pulmonary edema is always secondary to some other disease which usually originated in the cardiovascular system or in the lungs it is evident that the clinical background of any particular case is of the utmost importance in true evaluation of the situation

CONDITIONS IMMEDIATELY CONCERNED IN PRODUCTION OF ACUTE PULMONARY EDEMA

If the left ventricle of the heart is unable to propel blood from the thoracic cavity as rapidly as it enters the lungs the obvious effect is rapidly progressive and overwhelming acute pulmonary congestion This congestion may lead to acute pulmonary edema with startling rapidity Occasionally acute pulmonary edema will develop promptly early in the course of acute coronary thrombosis It is possible to make the error of attributing symptoms to pulmonary disease rather than to cardiac disease under these circumstances Whenever the syndrome of acute pulmonary edema develops rapidly and for the first time in a person who has been reasonably well previously the possibility of acute coronary thrombosis should be given consideration

PAROXYSMAL PULMONARY EDEMA

The syndrome of cardiac asthma and of paroxysmal nocturnal dyspnea is frequently ascribed to recurrent acute but temporary development of pulmonary edema Under these circumstances compensatory mechanisms of uncertain identity tend to develop and rescue the patient from development of fatal acute pulmonary edema It also has been suggested that the symptoms of orthopnea are due in part at least to postural edema The tendency toward pulmonary edema then is minimized when the patient is seated in an upright position because of the gravitational influences which inhibit the pooling of blood within the pulmonary circulation The symptoms of orthopnea cardiac asthma and paroxysmal nocturnal dyspnea occur in association with chronic congestive heart failure and the distress is undoubtedly due in part to an acute exacerbation of the chronic congestive state

Paroxysmal pulmonary edema also has been ascribed to angioneurotic edema associated with cutaneous edema The factors of laryngeal edema and possibly edema of the bron

chial mucosa may contribute to these symptoms but it is doubtful whether pulmonary edema in the common sense is produced by any allergic cause

EXCESSIVE BLOOD VOLUME

The phenomenon of acute pulmonary edema may develop as a result of excessive administration of intravenous fluids particularly in those cases in which acute renal failure with oliguria or anuria is present and the serum proteins are depleted

Acute pulmonary edema also somtimes results as a secondary phenomenon following administration of large volumes of blood or other intravenous fluids during shock which may occur during or after an extensive surgical procedure The combination of surgical shock and anesthesia may result in low blood pressure which requires transfusions but subsequent to operation when vascular tone is regained the artificially augmented blood volume may prove to be excessive and result in pulmonary edema especially among older patients who have limited circulatory reserve

PULMONARY INFLAMMATION

The increased capillary permeability which may develop as a result of extensive acute pulmonary disease such as pneumonia can lead to exudation of fluid into the air channels with development of symptoms of pulmonary edema Indeed this is a common cause of death in overwhelming pneumonia Milder and more temporary types of pulmonary edema which may be seen early in the course of severe acute pneumonia result from the congestion which precedes consolidation

The chemical inflammation produced by irritant gases is a well known cause of pulmonary edema The chemical damage to the alveolar membrane and pulmonary capillaries produced by the irritant gas which may be liberated in industrial accidents or in chemical warfare alters capillary permeability to such a point that blood plasma is permitted passage from the vascular channels into the air channels

PULMONARY METASTASIS

Not infrequently death from pulmonary metastasis is immediately attributable to the development of pulmonary edema as a terminal event The exact mechanism of this interference with pulmonary circulation is not entirely clear in many instances The factors involved might include obstruction to both vascular and air channels by masses of metastatic lesions and a severe state of anoxia which develops as a result of a loss of expansibility of pulmonary tissue when it is extensively involved by metastatic lesions with associated pulmonary fibrosis secondary bronchopneumonia cardiac failure and so forth

ANATOMIC, PHYSIOLOGIC AND ETIOLOGIC FACTORS

Examination of the structure of the lung suggests that pulmonary edema might be expected more frequently than it actually occurs in practice The great vascularity of the lung is probably unequaled by any other organ if the quantity of vascular tissue in relation to actual weight is considered The lung has an enormous capillary bed without the firm anatomic support which is seen in other vascular organs Furthermore the mechanical barriers between the vascular channels and the respiratory channels are necessarily delicate in structure in order to permit free interchange of gases The thin alveolar membrane and the delicate capillary endothelium are essentially all that separates blood from air and are the only barriers to transudation of fluid from the vascular tree into the tracheobronchial tree

Another factor requiring consideration is the fact that intrathoracic pressure is less than that of full atmospheric pressure especially during inspiratory phases of respiration This difference in pressure is greatest at the periphery of the lung near the potential pleural space and is least in the region of the trachea and the larger bronchi In the alveoli the negative intrathoracic pressure must be somewhere between these values but probably it is

more nearly that of intrapleural pressure. The entire vascular system of the systemic circulation, however, is under full atmospheric pressure. Pulmonary edema is more likely to occur under those conditions which increase the negative intrathoracic pressure.

The pressure in the pulmonary arteries is lower than that in the systemic circulation. The anatomic structure of the pulmonary vascular channels suggests that a greater degree of arterial pressure may be transmitted to the capillaries of the lung than to the capillaries in the greater circulation where the vessels involved are longer and the ultimate branching of arterial channels into capillaries is less promptly attained.

Severe hypoxia is a most frequent and important cause of pulmonary edema and it is equally true that pulmonary edema is a most potent factor in producing and accentuating hypoxia. The mechanical obstruction to the smaller air passages produced by the fluid which has seeped into the airway results in what is essentially drowning. This interference with free circulation of air in the alveoli rapidly results in the vicious circle. As the lung becomes more and more solid as a result of accumulation of fluid within the air passageways and with the associated inevitable thickening of interstitial structures from accumulation of fluid, there is a steady loss of elasticity so that free expansion and contraction of the lung are impossible to achieve. This reduction in pulmonary distensibility and elasticity seriously impedes the normal physiologic mechanisms which control the rate and depth of respiration because these are mediated through the central nervous system. The Hering-Breuer reflexes are interfered with seriously and the result is shallow, rapid breathing with incomplete aeration and further accentuation of the anoxia. It is well recognized that shallow breathing at a rapid rate is an exhausting and inefficient method of exchange of air and this of itself may lead to serious degrees of anoxia.

The permeability of the membrane separating the vascular from the respiratory channels is affected by chemical or bacterial inflammation. As soon as exudation of fluid occurs, free gaseous interchange is prevented and the resultant hypoxia will rapidly become an additional factor in the prevention of free interchange of gases.

There is considerable difference in the mechanical pressure which obtains in the finer vascular channels of the lung and the mechanical pressure within the alveoli. It is obvious that any factor which tends to increase the pressure within the vascular channels or to decrease the pressure within the air channels will increase the tendency toward passage of fluid through the intervening membranes.

Increase of blood volume to such an extent that venous pressure has increased may produce pulmonary edema, for the compensatory ability of the vascular system through the mechanism of vasodilatation has undoubtedly been exceeded. This important physiologic factor should be kept in mind when intravenous fluid, blood transfusions and so forth are being employed.

An extremely important factor in the retaining of fluid within the vascular channel is the osmotic pressure of the blood plasma. The most important factor in maintenance of this osmotic pressure is, of course, that produced by serum protein, especially serum albumin. Any disease which results in a striking decrease of osmotic pressure of the blood plasma will tend to decrease the effectiveness of an important mechanism for prevention of edema in the lungs and other organs. When renal failure occurs there is likely to have been a previous loss of albumin in the urine and abnormal retention of fluid.

As stated previously, any factor which tends to increase the negative intrathoracic pressure will have an effect of widening the difference between the pressure in the pulmonary capillaries and that in the pulmonary alveoli and will increase the tendency toward transmission of fluid through the intervening membrane from the area of higher pressure to that of lower pressure. When a large amount of fluid is withdrawn rapidly from the pleural space, the disturbed pressure relationship may rarely result in serious symptoms of pulmonary edema.

Excessive voluntary or involuntary inspiratory effort also may increase negative intra

thoracic pressure, and thus is thought by some to be a factor in production of "cardiac asthma" Indeed some persons can produce cardiac asthma by voluntary forced deep breathing The muscles of inspiration are much more powerful than the voluntary muscles of expiration so that the mean intrathoracic pressure during forced deep breathing is significantly reduced and may result in pulmonary edema but only if there is a delicate balance of other factors such as would be obtained in chronic congestive heart failure

There is considerable evidence that a true neurogenic form of pulmonary edema may occur Clinical evidence for this is furnished by the fact that pulmonary edema may be seen after acute head injury, intracranial surgical procedures epileptic seizures hypoglycemic shock and other disturbances of the central nervous system Anatomists demonstrate a rich supply of both afferent and efferent nerve pathways supplying both the vascular and respiratory channels of the lungs Much remains to be known about neurologic factors in the control of pulmonary circulation and in the control of pulmonary ventilation When these factors are more clearly elucidated it will be easier to understand neurogenic pulmonary edema

Treatment

Unquestionably oxygen therapy is the most important treatment available for incipient or actual pulmonary edema When symptoms of pulmonary edema have developed a serious degree of respiratory and circulatory decompensation has occurred and perhaps may have developed to an irreversible degree The proper time for oxygen therapy would have been before such serious symptoms as these had made their appearance Oxygen then must be considered even more important as a prophylactic agent in prevention of pulmonary edema than in the treatment of established pulmonary edema

The method of administering oxygen should be given serious thought in cases of pulmonary edema because undoubtedly such patients are in need of oxygen in its most concentrated and most direct form This makes it appear probable that an efficient oxygen mask should be used in preference to the oxygen tent because it is difficult to preserve a concentration of oxygen in an oxygen tent in excess of 50 to 60 % while with the mask concentrations closely approaching 100% may be administered readily The use of helium in combination with oxygen should be given serious consideration whenever there is obvious obstruction to the passage of air through the tracheobronchial tree

Positive pressure breathing utilizing either one of the several special devices available or calling upon an anesthesiologist to use his special equipment may be life saving in cases of pulmonary edema of whatever type The degree of pressure will have to be regulated according to the patient's tolerance Some types of apparatus can be regulated so as to cycle automatically without need for any effort or cooperation by the patient For types of equipment which do not cycle automatically manual control of the valve by a nurse in constant attendance may relieve the patient of the effort required to open and close the "demand valve

There are several reasons for the fact that breathing under positive pressure may prevent increase in pulmonary edema (1) The increased intrathoracic pressure produced may interfere with filling of the right side of the heart so that less blood actually enters the thoracic cavity If the left side of the heart retains sufficient ability to propel blood out of the thoracic cavity the tendency to accumulation and pooling of blood within the pulmonary circulation thus is lessened It should be indicated at this time that respiration under an excessive degree of positive pressure could result in inadequate filling of the right side of the heart with disastrous consequences (2) A second reason is that the increased intra-alveolar pressure produced in this artificial manner tends to offset the decrease in intrathoracic pressure to pathologic levels described in previous paragraphs Respiration under positive pressure can be considered to simulate a pressure bandage supporting the pulmonary circulation in a manner slightly similar to that by which an elastic bandage gives support to the circulation of an edematous leg (3) A third and important reason for the improved

clinical state of patients with pulmonary edema following treatment with positive pressure is that oxygen is being supplied in its most concentrated form by the most direct method and in abundant volume Larger amounts of oxygen are forced into the lungs past the obstructing fluid and into the alveoli where this gas is so desperately needed (4) A fourth possible reason for the clinical improvement after administration of oxygen under positive pressure is that of actual increase in the area of alveolar epithelium by a process of distention I doubt however whether this process is sufficiently extensive to play a significant role

The time honored practice of venesection occasionally may be lifesaving in cases of acute pulmonary edema Venesection has fallen into some disrepute because of its overenthusiastic use by former generations of physicians It is difficult to believe that physicians of former years continued to use venesection so freely without seeing some real evidence of therapeutic benefit. I have seen the temporary resuscitation of patients who apparently were dying from acute pulmonary edema by rapid withdrawal of 400 to 600 cc of venous blood

There is no medicinal treatment which appears to be of real benefit in pulmonary edema The use of atropine seems to be illogical since the fluid is not a glandular product and its formation is not inhibited by administration of atropine Morphine may be used on a humanitarian basis to relieve the patient of his distress but actually may do harm by dulling the sensitivity of the respiratory center and increasing the fatal trend to hypoxia

The inhalation of ethyl alcohol vapor with oxygen has been advocated as a method of reducing the surface tension of the obstructing mucus reducing bubble formation and facilitating expectoration This "anti foaming" effect can be realized conveniently by merely substituting 95% ethyl alcohol for water in the humidifying device of the oxygen supply equipment if the nasal catheter method of oxygen therapy is used If an oxygen mask is employed 30 to 40% ethyl alcohol is preferable Although there may be some mild sedation produced by the alcohol vapor there is no risk of actual intoxication

CHAPTER 16

Pulmonary Embolism

H Corwin Hinshaw, M D

Interest in the field of embolic phenomena remains at a high level due, in large part, to the sustained controversy concerning the use of anticoagulant drugs for coronary artery thrombosis Despite a large and growing literature there has been little fundamental or practical advance in this field as it relates to pulmonary embolism since the first edition of this volume was prepared in 1947 There has been extensive confirmation of the fact that pulmonary embolism is a frequent cause of death in medical and surgical diseases and that the premortem diagnosis remains difficult Many authors have urged the use of anticoagulant therapy in cases of known or suspected pulmonary embolism, yet none has completely demonstrated the degree of protection provided nor is there unanimity of opinion concerning the risks associated with treatment Selection of patients for treatment, duration of therapy and choice of drugs remain as topics for contention There is widespread agreement among students of this problem that "adequate treatment of "properly selected" cases with "accurate laboratory control" should (or will) "reduce the alarming mortality rate from pulmonary embolism"

FACTORS PREDISPOSING TO POSTOPERATIVE PULMONARY EMBOLISM

TYPE OF OPERATION

Operations for septic conditions and those associated with septic complications crushing injuries of the lower extremities, fractures or other conditions which necessitate immobilization, prolonged unconsciousness of whatever cause, prolonged and difficult surgery in the abdomen or pelvis and operations upon persons with predisposing medical conditions (advanced age cardiac disease, metastatic carcinoma, obesity and hematologic disorders) —all of these involve distinct risk of pulmonary embolism

Postoperative pulmonary embolism occurs after splenectomy more frequently than after any other operation possibly because of the associated disease of the hemopoietic system for which the splenectomy was performed Simple exploration for inoperable carcinoma associated with metastasis is another operation with high incidence of postoperative pulmonary embolism Usually the magnitude of the surgical procedure is directly related to the frequency of embolism, which is twice as common after repair of bilateral hernia as after operations for unilateral hernia

TRAUMA TO VEINS

Trauma to large veins may be an important factor in explaining the high incidence of embolism after pelvic or colonic operations or any intra abdominal operation of unusual difficulty, especially if it is associated with infection While pulmonary atelectasis is much more frequent after operations on the upper part of the abdomen than after other operations pulmonary embolism is more common after operations on the lower part of the abdomen Both embolism and atelectasis are

rare after operations on the head, neck or extremities

SEX

Both pulmonary embolism and atelectasis affect men much more frequently than women, despite the preponderance of operations on the lower part of the abdomen among women There is no completely adequate explanation for this sexual difference, although men are probably more dependent on muscles of the abdominal wall for respiration than are women and when these muscles are largely inactivated by an operation on the abdomen the flow of blood into the thoracic cavity is impeded Thrombophlebitis occurs after operation more frequently among women than among men but embolism to the lungs occurs more frequently among men than among women

STAGE OF POSTOPERATIVE CONVALESCENCE

Postoperative pulmonary embolism was commonly regarded as a very late complication of surgical treatment before adequate attention was given to the occurrence of premonitory, nonfatal episodes of embolism which so frequently precede the more severe manifestations by several days At least 25% of emboli will be noted during the first week after operation, 50% during the second week, and the remaining 25 per cent during the third and fourth weeks

PULMONARY EMBOLISM IN MEDICAL DISORDERS

CARDIAC DISORDERS

Cardiac disorders whether of arteriosclerotic, hypertensive, congenital or rheumatic nature predispose to pulmonary embolism in both medical and surgical patients Stagnation of blood flow is the usual basic cause for thrombosis and embolism The small emboli which originate from damaged heart valves and localized disease of the vascular intima constitute special problems, most commonly seen in endocarditis

THROMBOPHLEBITIS

Thrombophlebitis predisposes to pulmonary embolism but there are theoretical and practical reasons for believing that the clinical manifestations of peripheral thrombophlebitis are associated with such fixation of the thrombus by inflammation as to prevent subsequent massive pulmonary embolism When pulmonary embolism occurs after the clinical manifestations of thrombophlebitis have appeared the emboli are likely to be small and nonfatal It is more common to observe phenomena of pulmonary embolism a few days before clinical thrombophlebitis than after the symptoms of thrombophlebitis have appeared An excessive prolongation of convalescence after thrombophlebitis for prevention of late embolism does not appear justified and indeed such inactivity may tend to increase the danger of embolism When peripheral evidences of thrombophlebitis have subsided sufficiently to permit resumption of activity, any increased hazard of embolism has been passed Priestley and Barker reported an incidence of pulmonary embolism of 2% in 938 cases of thrombophlebitis, but in only 4 4% of cases did the embolism appear later than six days after the diagnosis of thrombophlebitis had been made

OBESITY

It is a well recognized fact, albeit incompletely explained, that pronounced obesity predisposes to thrombosis and embolism in both medical and surgical conditions Even minor obesity may contribute to this hazard following operations

VARICOSE VEINS

It is only surprising that thrombosis and embolism do not occur with greater frequency in persons with varicosities of the legs When such does occur it is often attributable to

local trauma or prolonged vein compression such as may occur during sleep in a sitting position during an all night airplane flight

AGE

One cause for the increased frequency of pulmonary embolism may be the increasing age of our population—thrombosis and embolism being relatively frequent in the aged and rare before the age of 40 years

METASTATIC MALIGNANCY

Occasionally a distinct "thrombophilia" is a striking feature of malignant disease even constituting the first clue to malignancy Clinically this is manifested by repeated episodes of thrombophlebitis and—following exploratory surgery—an excessive tendency to pulmonary embolism

SYMPTOMATIC DIAGNOSIS

The diagnosis of pulmonary embolism will depend frequently on clinical rather than on laboratory findings While roentgenographic and electrocardiographic studies are important and sometimes give extremely useful information these objective findings are sometimes absent or of nonspecific character Physical examination is also of accessory aid only the findings frequently being either absent or non specific The symptoms of pulmonary embolism are sufficiently characteristic however to permit clinical diagnosis to be made with reasonable accuracy While there is no one symptom which is pathognomonic of pulmonary embolism combinations of symptoms under proper circumstances may be thoroughly convincing that embolism has occurred

MASSIVE PULMONARY EMBOLISM

The clinical picture of massive fatal pulmonary embolism is well known Death may be extremely rapid often occurring before aid can be summoned Indeed an extremely rapid death especially if it occurs during convalescence from some medical or surgical disease is more likely to be due to pulmonary embolism than to a cardiac cause despite popular opinion to the contrary Nothing can terminate life more quickly than pulmonary embolism when the embolus is of such size as to occlude the pulmonary arteries almost completely with instant interruption of the circulatory stream although the size of the embolus is not always correlated with the severity of symptoms

If the patient who has massive pulmonary embolism lives sufficiently long to recite his symptoms he may describe sudden overpowering thoracic pain probably associated with dyspnea marked weakness and faintness and a horrible sensation of rapidly impending death Examination may reveal the classic findings of shock with weak rapid or imperceptible pulse gray cyanotic pallor difficult respiration and perhaps drenching cold perspiration Physical examination of the thorax may reveal nothing specific at this stage although respirations and cardiac rate will be rapid gallop rhythm may be noted and probably there will be an accentuation of the second pulmonic heart sound This clinical situation is obviously desperate and a poor prognosis will be given However if it is possible for the patient to survive for 24 hours with the aid of supportive treatment he has a reasonable chance of recovery if his original disease or operation has not drawn too heavily on his reserve

PULMONARY EMBOLISM WITH PLEURISY

Pleuritic pain which occurs after operation or other illness should lead to suspicion of pulmonary embolism if there is no other ready explanation This is especially true if the associated dyspnea appears to be out of proportion to restriction of respiratory movements imposed by the pain Experience demonstrates that simple pleurisy is probably one of the most frequent manifestations of pulmonary embolism and it is suspected that

rare after operations on the head, neck or extremities but embolism to the lungs occurs more frequently *among men than among women*

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such pain is more likely to occur when the embolus is small and reaches a peripheral pulmonary artery than when it is large. This type of pulmonary embolism is quite compatible with a normal sense of well being and an absence of any striking local or general symptoms or signs to suggest that such a potentially serious situation has developed. Sometimes the patient does not regard this symptom with sufficient interest to call his physician's attention to it, his only complaint being a pain in the thorax laterally on respiration. Physical examination may not reveal anything or perhaps there is a slight decrease of breath sounds on the affected side with limitation of excursion. A few hours later a pleuritic friction rub may be heard at times. Within a few days pleural effusion may occur.

When pleural effusion occurs after operation it should lead to suspicion that embolism has occurred if the abdominal operation has not involved any trauma to the diaphragm and there is no other explanation for the occurrence of an effusion. When an effusion follows what was thought to be postoperative "pneumonia" or "atelectasis," I often review the situation from the beginning and sometimes secure evidence that the original diagnosis was in error and that the lesion was of embolic origin.

No one can deny the possibility that simple "pleurisy" may occur after operations but we believe that such a diagnosis should be made rarely because pleuritic pain is nearly always indicative of underlying pulmonary pathologic processes. It is of course necessary to distinguish sharply between true pleurisy and thoracic pain of mural origin. If the patient states that his thoracic pain resembles that which he has experienced prior to his present illness, if it is of dull character and not strictly related to respiratory movements and if it does not actually hinder full deep inspiration, then it is improbable that he is suffering from the true pleuritis. Actual pleural inflammation will yield a very striking sharp readily identified and localized type of pain which occurs on inspiration and is largely or totally relieved when respiration is interrupted as when the physician's hand firmly prevents expansion in the affected region.

The great importance of recognizing the occurrence of small pulmonary emboli is obvious. It indicates that thrombosis has occurred somewhere with resultant embolism and it is to be feared that the process will continue with grave danger of subsequent massive pulmonary embolism.

"PNEUMONIC" TYPE OF PULMONARY EMBOLISM WITH INFARCTION

Occasionally patients who have survived the initial stages of a rather large pulmonary embolism will suffer from a prolonged febrile illness lasting for 3 or 4 weeks or more with sustained high fever. If the initial stages of this illness are atypical or are interpreted incorrectly, the patient may be treated as though he were suffering from some infection which may be assigned incorrectly to his operation or original illness or to postoperative "pneumonia." The latter impression may be heightened by roentgenographic evidences and physical signs of pulmonary consolidation and possibly subsequent pleural effusion. Such a febrile illness may be due to a large pulmonary infarct which may or may not break down to produce pulmonary abscess.

HEMOPTYSIS IN CASES OF PULMONARY EMBOLISM

Occasionally hemoptysis is the first symptom which clearly indicates pulmonary embolism. When the expectoration of blood is noted after operation or in connection with some extrathoracic disease this sign should be regarded as very strong evidence of pulmonary embolism. Usually a review of the clinical situation will reveal that other symptoms of pulmonary embolism have also been present, such as pleural pain, dyspnea, mild symptoms of shock with tachycardia, fever and so forth. Often the expectoration consists of almost pure blood which usually is clotted and rather small in amount. I have not seen massive hemorrhage from pulmonary embolism. The blood is not likely to be of fresh appearance or frothy in consistency. Hemopty

sis of other origin is described frequently as effortless welling up in the throat of blood which suddenly appears and which may be in considerable quantity The hemoptysis associated with pulmonary embolism is usually somewhat different and consists of the coughing up and expectoration of a thick bloody sputum The blood is likely to be rather dark and clotted in appearance when it first is noted and the blood becomes darker and scantier from day to day There is no other postoperative pulmonary complication which is likely to yield this type of sputum and we believe that such symptoms usually should be regarded as evidence of pulmonary embolism In such instances corroborative evidence will usually be secured on review of previous clinical symptoms on roentgenographic and electrocardiographic studies on physical examination and on subsequent course of the illness

It must be emphasized that hemoptysis is not essential to the clear establishment of a diagnosis of pulmonary embolism and only a minority of patients who have pulmonary embolism actually expectorate gross blood It obviously is essential that the physician exclude any possibility that the expectorated blood was derived from epistaxis with subsequent aspiration into the tracheobronchial tree

NERVOUS SYMPTOMS

The violent psychic symptoms of massive pulmonary embolism have been mentioned in a previous paragraph but I have seen occasional instances of nonfatal pulmonary embolism in which the initial symptoms were referable to the central nervous system and at first were thought not to be of any serious consequence Such patients have experienced sudden feelings of apprehension anxiety and palpitation with dyspnea perhaps in association with their earliest excursions from bed after an operation The associated weakness and dyspnea often have been so severe as to make it impossible for them to get back into bed without assistance By the time a physician has reached the bedside the patient may be feeling well and since there is no objective finding to establish a diagnosis the whole episode may be regarded as one of functional nature However a few hours later a pleuritic pain may develop or hemoptysis may occur a day or two later or electrocardiographic or roentgenographic studies may subsequently reveal the presence of pulmonary embolism Review of the situation with particular reference to nurses bedside notes will appear to establish the fact that the original manifestation of embolism was probably one which appeared to be entirely nervous in character While it does not seem that such an episode of apprehension should be taken as convincing evidence of embolism such patients should be watched with especial care for development of corroborative symptoms or signs which may establish the fact that embolism did occur and lead to prompt appropriate treatment for the prevention of a subsequent and more serious attack

OTHER SYMPTOMS

I have rarely encountered abdominal pain and rigidity as an outstanding feature of pulmonary embolism In the few instances in which these symptoms were present the thoracic pain extended over the upper part of the abdomen to a striking degree with associated boardlike rigidity of the abdominal muscles and symptoms of shock so striking as to lead to suspicion that some intra abdominal catastrophe had occurred such as rupture of a viscus The diagnosis of embolism became obvious later when the pain retreated to the thoracic wall alone and other more classic symptoms and findings of embolism developed

Early symptoms of pulmonary embolism may be so predominantly cardiac in type as to lead to the incorrect assumption that primary cardiac disease is present The syndrome of "acute cor pulmonale" is essentially that described in a previous paragraph when the massive type of pulmonary embolism was being discussed The right ventricle is called on suddenly to propel the full stream of blood through a channel narrowed by the presence of an embolus In addition there may be an associated factor of vasoconstriction in smaller pulmonary vessels which further impedes the

flow of blood, leads to rapid dilatation of the right ventricle and contributes to eventual cardiac failure, which is the ultimate cause of death in massive pulmonary embolism

In other instances the early symptoms of pulmonary embolism may be entirely those of cardiac strain with increased cardiac rate and a subjective sense of palpitation with dyspnea and, possibly, the physical finding of gallop rhythm These symptoms alone are not adequate to justify a diagnosis of pulmonary embolism unless there are convincing electrocardiographic signs or subsequent development of other symptoms more characteristic of pulmonary embolism

It must be emphasized that it is rare for pulmonary embolism to be manifested by any one of the preceding symptoms alone Usually several of the foregoing symptoms exist simultaneously or develop in sequence each one strengthening a diagnosis which at first may have been only tentative and uncertain The clinician is urged to be continually aware of the possibility of pulmonary embolism so as to establish the diagnosis at the earliest possible hour He may first note merely a minor attack of nervousness with apprehension and palpitation, which of itself does not have any conclusive diagnostic value However, if pleural pain develops a few hours later, the original symptom takes on added significance and, if subsequently hemoptysis occurs, if a shadow suggesting pulmonary embolism is seen on roentgenographic examination of the thorax and if later pleural effusion makes its appearance and electrocardiographic findings of embolism appear, the original tentative diagnosis is receiving steadily increased reinforcement and at some stage of this sequence treatment should be instituted in an attempt to prevent subsequent fatal embolism

ASYMPTOMATIC PULMONARY EMBOLISM

The pathologist occasionally will find evidence of recent or ancient pulmonary embolism in post-mortem examination of patients who have died of other disease Sometimes a critical review of a most complete clinical record will fail to yield any evidence of subjective symptoms or objective manifestations of the embolism which the pathologist has demonstrated While the symptoms may have occurred and been wrongly interpreted or the patient may have failed to describe his subjective sensations, it still seems probable that pulmonary embolism may occur in the absence of all symptoms and objective manifestations While such asymptomatic emboli are usually small, they are sometimes surprisingly large and even may be associated with rather extensive pulmonary infarction

PHYSICAL EXAMINATION

Physical examination may or may not be rewarding Increased cardiac rate, rapid respiration, diminished blood pressure, pulmonary rales, and accentuation of the second pulmonic heart sound may provide useful diagnostic clues. The findings of pulmonary consolidation pleural friction rub, and possible pleural effusion are delayed and very frequently never appear Fever usually is present but is likely to be ascribed to the preceding medical or surgical condition

ELECTROCARDIOGRAPHIC FINDINGS

In a majority of cases the electrocardiogram provides no helpful clues to the diagnosis of pulmonary embolism However, if signs of right ventricular strain are recorded and especially if these were known to be absent previously, strong presumption of pulmonary embolism may be assumed if the clinical situation is compatible with such a diagnosis The distinction between myocardial infarction and pulmonary embolism may be very difficult and errors have been made by skilled physicians [38] The findings of right heart strain (acute cor

pulmonale) may be transient appearing within a few hours and disappearing within a day or two (The reader is referred to page 354 for descriptions of the changes found in the electrocardiogram in right ventricular heart strain)

ROENTGENOGRAPHIC DIAGNOSIS OF PULMONARY EMBOLISM

While a specific type of roentgenographic picture has been described for pulmonary embolism it is by no means essential to a definite diagnosis The roentgenographic picture which occurs most frequently could best be described as unilateral chronic passive congestion with accentuation of the vascular trunks of one side or one lobe This is likely to be associated with elevation of the hemidiaphragm on the affected side and perhaps later with obliteration of the corresponding costophrenic angle However if an abdominal operation has been performed elevation of the diaphragm as a solitary finding cannot be given any great emphasis Frequently a mottled or patchy type of infiltration indistinguishable from postoperative atelectasis or pneumonia may be seen and at later stages of development the presence of pleural effusion will draw attention to the possibility of embolism It must always be remembered that asymptomatic postoperative atelectasis may occur and produce confusing shadows indistinguishable from those of pulmonary embolism

TREATMENT OF PULMONARY EMBOLISM

SUPPORTIVE AND SYMPTOMATIC MEASURES

Massive pulmonary embolism constitutes an acute medical emergency requiring very active and immediate treatment Administration of oxygen usually is imperative and sometimes may be lifesaving Oxygen should be administered by the most efficient and direct method possible and in the greatest concentration obtainable For these reasons there is advantage in the use of an oxygen mask utilizing pure oxygen in preference to the oxygen tent in which the concentration of oxygen cannot be maintained at more than 50 or 60% I have seen patients markedly improve when changed from the oxygen tent to the oxygen mask There is a possibility that the ice cooled air to the tent could produce reflex vasospasm in the lesser circulation and an increased tendency to bronchospasm

The use of papaverine was advocated as early as 1927 by Barnes and has gained acceptance because of clinical improvement which has followed There is experimental evidence that this drug effectively combats the alleged tendency to reflex constriction of vessels in the pulmonary circulation Atropine has theoretical and practical advantages and it is my belief that this drug should be employed routinely The intravenous administration of $^1/_2$ grain (0 032 gm) of papaverine and $^1/_{100}$ grain (0 00065 gm) of atropine as soon as possible after massive pulmonary embolism occurs is suggested If morphine is necessary it should be used cautiously in patients who have received papaverine the two drugs acting together to depress respiration

ANTICOAGULANT THERAPY

The decision to employ anticoagulant therapy will depend upon the physician's estimate of the risk of subsequent embolism his confidence in the drug as a prophylactic agent and his estimate of the risk that hemorrhage might occur as a result of treatment Since the clinician will depend heavily upon his laboratory colleagues for guidance of therapy his choice may well depend upon his confidence in the laboratory especially when the dicumarol types of drugs are considered

Heparin is the widely preferred anticoagulant in many circumstances because of its prompt action relative safety efficacy and

ease of management. Repository preparations of the drug are now available which replace the intravenous injections formerly recommended. Subcutaneous injections—into the fat of the thigh preferably—once or twice daily are given in sufficient amount to maintain a coagulation time (Lee White method) of 30 to 60 minutes (normal 9–15 minutes). This usually requires an initial dose of 30 000 to 40 000 International units followed by daily doses of about 20 000 units. Each dose is preceded by a determination of the coagulation time.

Dicumarol has the small advantage of oral medication but its regulation is much more difficult than in the case of heparin. The dosage requirements vary considerably and must be determined daily by estimation of the prothrombin time. The latter test is difficult and is often performed inaccurately in laboratories which are otherwise quite dependable. Errors in dosage may have catastrophic effects: hemorrhage which is difficult to control. Usually an initial dose of 300 mg of dicumarol is recommended followed by daily doses adequate to maintain a prothrombin time of about twice that of a control sample of blood. Several additional preparations designed to overcome some of the disadvantages of dicumarol have been proposed in recent years and each has its advocates with apparent good reason. These include such preparations as Phenylindanedione, Warfarin sodium, Marcumar, Tromexan, Phenylpropylhydroxycoumarin, Acenocoumarin, Cyclocumarol and others.

Anticoagulants of either type should be continued for one to three weeks after the last suggestive evidence of embolism.

PREVENTION OF THROMBOSIS

The virtues of preventive measures to avoid the misfortune of thrombosis need not be extolled. The foremost of these measures is early ambulation following surgery, but this is by no means a panacea for thrombosis and embolism continue to appear even after very early ambulation.

PREVENTION OF VENOUS STASIS

It has been suggested by Barnes and others that some effort to prevent pulmonary embolism should be made in the cases of many patients who are in excess of 40 years of age, especially if there be any reason to suspect cardiovascular disease. Efforts to prevent venous stasis may be made in all cases. Since venous stasis in the lower extremities is most likely to lead to thrombosis and pulmonary embolism, it is urged that special care be taken to keep the lower extremities of all patients warm and adequately exercised. If the temperature of the skin is maintained at 86°F or above, essentially complete vasodilatation will be accomplished. If the patient is encouraged to undertake voluntary exercises with his lower limbs the danger of stasis will be further decreased. Movements of the legs simulating those of bicycle riding are frequently recommended and these should be repeated several times during the day. Passive massage of the lower extremities, particularly of patients who have cardiac disease, has been advised.

RESPIRATORY ACTIVITY AND VENOUS FLOW

Since the alternating negative pressure within the thorax serves not only to propel air in and out of the lungs but also to propel blood into the thorax, it is believed that deep breathing exercises or stimulation of deep respiration by inhalations of carbon dioxide will also be of benefit. Such deep breathing is also highly desirable for postoperative patients to prevent the development of atelectasis. These are procedures which may be placed on a routine basis and carried out methodically by nurses, essentially without expense or hazard. It is our belief that they should be employed more widely for both surgical and medical patients than they are at present.

LIGATION OF THE FEMORAL VEIN

Ligation of the femoral vein has often been recommended yet has retained its popularity in few medical centers It has appeared to be most effective when combined with anticoagulant therapy but results seem to be similarly favorable with anticoagulants alone Unfortunately thrombosis proximal to the point of ligation may occur if anticoagulants are not administered Under extreme circumstances even the inferior vena cava has been ligated to control repeated embolism

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ease of management. Repository preparations of the drug are now available which replace the intravenous injections formerly recommended. Subcutaneous injections—into the fat of the thigh preferably—once or twice daily are given in sufficient amount to maintain a coagulation time (Lee White method) of 30 to 60 minutes (normal 9–15 minutes). This usually requires an initial dose of 30 000 to 40 000 International units followed by daily doses of about 20 000 units. Each dose is preceded by a determination of the coagulation time.

Dicumarol has the small advantage of oral medication but its regulation is much more difficult than in the case of heparin. The dosage requirements vary considerably and must be determined daily by estimation of the prothrombin time. The latter test is difficult and is often performed inaccurately in laboratories which are otherwise quite dependable. Errors in dosage may have catastrophic effects, hemorrhage which is difficult to control. Usually an initial dose of 300 mg. of dicumarol is recommended followed by daily doses adequate to maintain a prothrombin time of about twice that of a control sample of blood. Several additional preparations designed to overcome some of the disadvantages of dicumarol have been proposed in recent years and each has its advocates with apparent good reason. These include such preparations as Phenylindanedione, Warfarin sodium, Marcumar, Tromexan, Phenylpropyl hydroxycoumarin, Acenocoumarin, Cyclocumarol and others.

Anticoagulants of either type should be continued for one to three weeks after the last suggestive evidence of embolism.

PREVENTION OF THROMBOSIS

The virtues of preventive measures to avoid the misfortune of thrombosis need not be extolled. The foremost of these measures is early ambulation following surgery, but this is by no means a panacea for thrombosis and embolism continue to appear even after very early ambulation.

PREVENTION OF VENOUS STASIS

It has been suggested by Barnes and others that some effort to prevent pulmonary embolism should be made in the cases of many patients who are in excess of 40 years of age, especially if there be any reason to suspect cardiovascular disease. Efforts to prevent venous stasis may be made in all cases. Since venous stasis in the lower extremities is most likely to lead to thrombosis and pulmonary embolism it is urged that special care be taken to keep the lower extremities of all patients warm and adequately exercised. If the temperature of the skin is maintained at 86°F or above, essentially complete vasodilatation will be accomplished. If the patient is encouraged to undertake voluntary exercises with his lower limbs the danger of stasis will be further decreased. Movements of the legs simulating those of bicycle riding are frequently recommended and these should be repeated several times during the day. Passive massage of the lower extremities, particularly of patients who have cardiac disease, has been advised.

RESPIRATORY ACTIVITY AND VENOUS FLOW

Since the alternating negative pressure within the thorax serves not only to propel air in and out of the lungs but also to propel blood into the thorax, it is believed that deep breathing exercises or stimulation of deep respiration by inhalations of carbon dioxide will also be of benefit. Such deep breathing is also highly desirable for postoperative patients to prevent the development of atelectasis. These are procedures which may be placed on a routine basis and carried out methodically by nurses. It is essentially without expense or hazard. It is our belief that they should be employed more widely for both surgical and medical patients than they are at present.

LIGATION OF THE FEMORAL VEIN

Ligation of the femoral vein has often been recommended yet has retained its popularity in few medical centers It has appeared to be most effective when combined with anticoagulant therapy but results seem to be similarly favorable with anticoagulants alone Unfortunately thrombosis proximal to the point of ligation may occur if anticoagulants are not administered Under extreme circumstances even the inferior vena cava has been ligated to control repeated embolism

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CHAPTER 17

Atelectasis

ANDREW L BANYAI, M D

ATELECTASIS is defined as airlessness of smaller or larger areas of the lung which is not caused by exudate, transudate or tumor tissue filling the alveoli or by fibrous tissue obliterating the air cells

Most cases of clinically significant atelectasis are acquired Congenital atelectasis occurs in premature infants due to weakness and functional incompetence of the respiratory muscles Also, atelectasis may be caused by undue softness of the supportive structures of the thorax, immature, uninflatable lung lobules, underdevelopment and inadequate function of the respiratory center or depression of the latter by intracranial stasis or general hypoxia Atelectasis may exist in infants born at term in whom respiratory function is inadequate on account of developmental defects of the diaphragm, disturbance in the respiratory center due to intracranial hemorrhage or as the result of aspiration of foreign material (amniotic fluid mucus or blood) into the lung Intracranial hemorrhage may lead to atelectasis either by hypoventilation caused by pressure upon the respiratory center or by reflex contraction of the pulmonary smooth muscles

Atelectasis may be classified in the following categories (1) According to extent Massive, lobar, patchy, linear, nodular (2) According to location Unilateral, bilateral According to onset Sudden, slow According to duration Acute, subacute, chronic According to its course Reversible (transient, temporary), Irreversible (permanent)

The extent of atelectasis is influenced by the size of the respiratory passage which becomes occluded Also, it is effected by the degree of failure of the respiratory function Lobar atelectasis may be brought about by blockage of one large bronchus or several smaller bronchi

Bronchi may become blocked by viscid, tenacious secretions, mucous plugs, fibrin, edema of the mucous membrane, granulation tissue, fibrous stenosis, new growth, external compression and by reflex spasm Not infrequently a combination of some of these factors is responsible for the development of atelectasis The latter may be brought about by local hypersecretion of mucus in certain areas or bronchial secretions or inflammatory exudate may spill from one site of the lung to another Occasionally a thin but viscous film of mucus may settle across the lumen of the bronchus and may lead to atelectasis The latter may promptly clear when this obliterating film breaks up, possibly to recur when a new viscid film of exudate occludes the bronchus

Conditions and diseases in which atelectasis may be encountered include the following postoperative states, aspiration of foreign bodies, trauma to the chest or severe trauma elsewhere, pneumonia, pulmonary hemorrhage from any cause, bronchial asthma, bronchiectasis, lung abscess, severe bronchitis and bron-

neoplasms of the mediastinum, esophagus, heart, chest wall and abdomen, large intrathoracic cysts (congenital, echinococcus, dermoid), enlarged thymus, congenital substernal goiter, thoracic aneurysm, massive enlargement of tracheobronchial lymph nodes (infection neoplasm, silicosis, leukemia), enlargement of the heart, duct of Cuvier, large pericardial effusion, pneumothorax, large pleural effusion

or mediastinal effusion acute painful diseases of the diaphragm paravertebral cold abscess anomalous bronchi deformity of the chest wall rickets with weakness and functional incompetence of the chest wall injury to the phrenic nerve with paraylsis of the diaphragm injury to the vagus nerve with consequent reflex bronchospasm large ascites and severe acute abdominal disease (peritonitis pancreatitis) hemorrhage or edema of the brain acute meningitis acute encephalitis poliomyelitis coma due to brain trauma uremia diabetes epilepsy or other causes severe burns pronounced debility due to myasthenia gravis old age starvation chronic infections and other causes

The interplay of several factors is instrumental in the development of postoperative atelectasis Among these mention should be made of the following possibilities (1) Reflex inhibition of the respiratory excursions of the diaphragm (2) Reflex spasm of the peribronchial and peribronchiolar smooth muscles attributable to irritation of the vagus nerve during major abdominal operations (3) The deeper the anesthesia the more likely its possible depressive effect upon respiratory function and pulmonary expansion (4) Respiratory excursions of the diaphragm are smaller in the recumbent position than in the upright position In the supine position the lung volume is reduced by about 20% The intrapleural pressure is less negative in the recumbent position (5) Under deep general anesthesia there may be pronounced interference with normal bronchial peristalsis and with the normal ciliary function of the bronchial mucosa The resulting deficient bronchial drainage (bronchocatharsis) is likely to lead to stagnation and accumulation of secretions and thus to occlusion of the lower air passages (6) Preoperative and postoperative administration of opium derivatives in unduely large doses is bound to depress the respiratory center and render the respiratory excursions of the chest inadequate The consequent decrease in the size of the lung bronchi and bronchioles may facilitate the development of atelectasis Additional drawbacks of opiates are in this respect (1) diminution of bronchial peristalsis (2) slowing down of ciliary function (3) suppression of cough reflex The latter is the most harmful of the three

The incidence of postoperative atelectasis is higher in smokers than in nonsmokers It is more frequent in heavy smokers than in light smokers Substances present in tobacco smoke inhaled are irritating to the bronchial mucous membrane Also nicotine has a direct adverse influence A great many smokers develop manifest or subclinical chronic bronchitis The chronically inflammed and edematous mucosa narrows the caliber of the lower air passages and thereby renders their occlusion easier Moreover nicotine exerts a vasopressor effect upon the branches of the bronchial artery Contraction of the nutritional blood vessels of the bronchial mucosa is bound to lower the latter s defense capacity Consequently the propagation of pathogenic microorganisms inhaled or aspirated from the oropharynx is facilitated The ensuing inflammatory process accelerates the development of bronchial blockage Also it is known that tobacco smoke stimulates the secretions of the bronchial mucosa thus directly increasing the chances for subsequent occlusion of some of the bronchial branches There are an associated slowing of bronchial peristalsis and retardation of ciliary function

Aspiration of material from the upper air passages into the lung during general anesthesia deserves due consideration because it may result in bronchial infection mucosal edema and atelectasis The postoperative train of events in reference to atelectasis is influenced in no small measure by the patient s disinclination to take deep breath because of pain This instinctive hypoventilation sets up a chain of events which are favorable to the development of atelectasis To this there is added the patient s abstention from coughing so as to avoid pain in the region of surgical intervention Cough is the body s most expedient weapon for ridding the respiratory tract from accumulated mucus aspirated material and inflammatory products In its absence a vicious circle is bound to develop atelectasis may follow the retention of these substances Atelectasis in turn weakens or nullifies the efficacy of cough Old de

bilitated individuals and patients *with heart failure* are more likely *to develop atelectasis* postoperatively *than others*

Trauma to the chest wall or to the lung even in the absence *of perforating* wounds *may be followed by atelectasis Factors which are thought to* be responsible for bringing about atelectasis *include* (1) chest *pain* with consequent shallow respiration and *tussive insufficiency* (2) reflex bronchospasm (3) small intrabronchial or peribronchial hemorrhages (4) possible pleural effusion *with* consequent compression of the lung parenchyma (5) abdominal ileus may ad*versely effect the respiratory motion of the* diaphragm and pulmonary ventilation Atelectasis may develop in the lung opposite to the site of blunt trauma to the chest Also it may follow crushing injury to the thigh pelvis or *other extrathoracic parts of the body*

In pulmonary hemorrhage bronchial occlusion by a blood clot seems to explain the development of atelectasis However it is well to bear in mind the existence of a reflex which brings about spastic contraction of the regional bronchi in response to pressure exerted by the *extravasated blood upon the nerve endings* of the vagus

Atelectasis may set in during the course of bronchial asthma in consequence of bronchospasm mucosal swelling and occlusion of the bronchi by tenacious secretions

In diseases of the central nervous system which are accompanied by depression of the respiratory center the patient is in danger because of the ensuing hypoventilation decrease in the size of the lung and of the patency of bronchi aspiration of mucus from the upper *air passages and tussive insufficiency*

Pronounced kyphoscoliosis and other severe deformities of the chest wall massive intrathoracic tumors and large pleural pericardial mediastinal and peritoneal effusions not only compress the lung but also seriously interfere with the normal cough mechanism

Ponopnea (painful inspiration) in association with acute diseases of the diaphragm explains the limitation in motion of this muscle and the possible consequent development of nodular or plate like" atelectasis

Atelectasis in patients with poliomyelitis *occurs during* or after the acute phase Cases have been observed as late as few weeks to *one year after the termination of the acute* illness

Severe burns may induce atelectasis either on account of painful respiration or in a reflex manner namely by spastic occlusion of some *of the bronchi*

In shock (*surgical medical or traumatic*) the greater the shock the less *negative* the intrapleural pressure The consequent inadequate respiratory excursions of the lung are predilectional to the development of atelectasis

Atelectasis is more common in the posterior dependent parts of the lung The role of gravity topography of the bronchi as free channels for aspirated mucus inflammatory exudate and *foreign bodies as well as limitation* in motion of the diaphragm under certain circumstances readily explain this situation *Both lower lobes may become atelectatic* The ratio of involvement of one entire lung to that of one of the lower lobes is approximately 1 4 Atelectasis of the right middle lobe is readily produced by occlusion of its bronchus *which is narrow and leaves the main bronchus* at an acute angle

Kerley called attention to the frequency with which atelectasis develops in the fourth (accessory) lobe of the right lung He attributed this to the fact that the connecting bronchus of this lobe frequently branches off the paracardial bronchus of the right lower lobe The paracardial branch is a bronchus of third degree and as such it contains only irregular fragments of cartilage and *thus it* becomes easily occluded Accessory lobe on the right side occurs in from 15 to 20% of normal individuals The incidence of accessory lobe on the left side is about 15%

The atelectatic lobe is *markedly* reduced *in* size and it is functionless Fibrosis *is bound* to develop rapidly *when* atelectasis is complicated by infection In massive atelectasis the intrapleural pressure may reach minus 44 cm of water on inspiration and minus 33 cm of water on expiration the corresponding normal figures are −7 and −2 respectively

A number of complications *may be en*countered in atelectasis Of these *the inci*

dence of pneumonia is high Bronchiectasis is a frequent and serious complication In some instances the virulence and the large number of pathogenic micro-organisms retention of foreign body the lowered vitality of the affected region and its functional incompetence may result in abscess formation Compensatory emphysema appears early in the unaffected surrounding lung zones or in the opposite lung Massive atelectasis may be followed by pleural effusion Usually it is hemorrhagic in character

SYMPTOMS

Symptoms of atelectasis are greatly influenced by the pathogenesis and extent of the lesion Atelectasis of large portions of the lung which develops after aspiration of foreign bodies postoperatively or in other forms of acute bronchial occlusion is accompanied by abrupt onset of pronounced symptoms There is a sudden urgent intense dyspnea with tachypnea The patient may be found sitting up in bed obviously in acute respiratory distress Anxiety and profuse perspiration together with restlessness may be noted The extreme dyspnea lasts for several hours At the same time the patient may complain of a sense of discomfort or sharp pain in the affected side or over the sternum Cyanosis becomes evident early and it is exaggerated during cough Cyanosis may be absent however when bronchial occlusion develops slowly Cough is usually unproductive in the beginning It is of short hacking character Later it becomes productive of tenacious mucoid or mucopurulent expectoration Chills and fever may usher in the disease In a great many postoperative cases the onset of this condition is less dramatic However the occurrence of otherwise unexplained fever elevation of pulse rate and respiratory rate within 48 hours after operation should bring to mind the possibility of atelectasis Elevation of temperature is usually moderate although it may reach 103°F There are instances in which fever is entirely absent

Not infrequently it is noted that dyspnea and cyanosis are out of proportion to the loss of respiratory area As an explanation in this regard the following factors are to be considered The blood passing through the atelectatic region is not oxygenated because bronchial obstruction prevents entry of tidal air to the corresponding alveoli There is a diminution in the ventilatory and respiratory function of the affected lung even when one lobe is atelectatic This functional insufficiency is caused by the high position and lack of motion of the corresponding hemidiaphragm The same influence is exerted by decrease in the size of the hemithorax on the same side Due to the upward displacement of a hemidiaphragm there develops a functional imbalance between the right and left halves of the diaphragm With the fixation of the high hemidiaphragm on the affected side the normal function of the opposite side may be interfered with Moreover the inspiratory descent of the hemidiaphragm on the sound side forces the abdominal organs into the thorax on the opposite side and thereby adds to the further reduction of the lung volume The healthy lung opposite to the one with atelectasis loses some of its respiratory competence due to influx of stale stagnating air from the affected lung Displacement of the heart and large mediastinal blood vessels may seriously interfere with circulation Thus circulatory embarrassment is added to respiratory difficulties Similar influence is exerted by the highly negative intrapleural pressure in massive atelectasis It creates a steep centripetal gradient increased blood flow toward the thorax

DIAGNOSIS

Findings in atelectasis vary greatly They are determined by the site and extent of involvement by the underlying pulmonary disease the presence or absence of pronounced

compensatory emphysema and by pathologic changes caused by possible *complications* Fever is accompanied by rapid pulse and increased respiratory rate The latter is often out of proportion to physical findings In *massive and in acute lobar atelectasis* one finds decrease in the size and absence or limitation in motion of the affected hemithorax The intercostal spaces are narrowed and depressed In atelectasis of one of the upper lobes, palpation may reveal shift of the trachea toward the diseased side There is dullness or flatness to percussion On percussing the chest particular attention should be paid to the paravertebral area at the base and to the cardiohepatic angle where atelectatic lobes of these regions have a tendency to retract The liver dullness is high in extensive atelectasis on the right side Respiratory motion of the corresponding hemidiaphragm is absent In massive atelectasis on the left side, tympanitic percussion note can be elicited much higher than normally over the lower part of the chest due to the upward displacement of the stomach Pectoral fremitus cannot be detected over the involved area The apical impulse of the heart is displaced toward the site of atelectasis when one of the lower lobes is involved Auscultatory findings are corroborative in this respect In massive atelectasis, the uninvolved lung is hyperresonant to percussion, shows increased respiratory excursions and accentuated breath sounds In contrast, over the atelectatic lung, the breath sound and whispered voice conduction are absent Sonorous and sibilant rales may be detectable over the surrounding lung Subsequently, bronchial or tubular breathing is audible over large areas of atelectasis Variations in physical findings are frequently seen in lobar atelectasis This phenomenon is attributable to differences in the degree of bronchial occlusion and to the potential reversibility of early atelectasis With the onset of complications (pneumonia, abscess, bronchiectasis), there is a change and augmentation in physical findings It was pointed out by de Takats and his associates that patients with right lower lobe atelectasis often show right upper rectus rigidity

Roentgenologic findings are of utmost importance in clarifying the diagnosis Inasmuch as x-ray films taken in the standard projection may fail to reveal atelectasis, it is advisable to take roentgenograms in the lateral and oblique positions Tomograms (anteroposterior and lateral) are of value for the demonstration of atelectasis By fluoroscopic examination one is able to observe the *Holzknecht-Jakobsohn sign* shift of the heart toward the diseased side on inspiration and its return to its original position on expiration Too, in early atelectasis, the respective hemidiaphragm can be observed under the fluoroscope as it moves upward during inspiration In general, radiographic examination reveals the following findings in massive and in lobar atelectasis

(1) Decrease in the size of the hemithorax on the affected side, depending upon the extent of involvement

(2) Increased slanting of the ribs

(3) Decrease in the width of intercostal spaces

(4) In early cases there is a mottling in one lobe or one lung which becomes confluent, homogeneous, dense or presents a ground glass appearance subsequently

In lobular atelectasis there is a nodular, miliary like appearance.

Segmental atelectasis recognized from shadows which topographically correspond to the normal anatomic sites of these units The size of the individual segment is reduced and its shape may be quadrangular, disk like, wedge-shaped, patchy ill defined or narrow band like

Atelectasis of an entire lobe may be seen as a triangular shadow in the standard roentgenogram The base of the triangle is at the periphery, its mesial border merges with the shadow of the spine or may be obscured by the heart shadow when a lower lobe is involved, its lateral border or hypotenuse forms a sharply defined, slightly convex, straight or concave line which extends from the hilum to the base of the triangle In this area the bronchovascular markings are placed closer than in the corresponding sound regions of the lung Atelectasis of the right middle lobe may not be seen in a standard roentgenogram because the shrunken lobe is hidden by the dome of the diaphragm When this is the

case an x ray film taken in the lordotic position will reveal the lesion Simultaneous collapse of the right lower and middle lobes is as a rule represented by a triangular shadow The occurrence of bilateral basal triangular shadows corresponding to atelectasis of both lower lobes is very rare

(5) Emphysema of the surrounding lung is recognized from increased radiotranslucency and by a wider spread of bronchovascular markings than seen normally

(6) An apico basal displacement of the hilar shadows is noted in atelectasis of an upper or lower lobe The displacement is toward the affected lobe Consequently parts of the hilar structures may become obscured by mediastinal organs or by the involved lung and thus the hilum may appear decreased in size Displacement of the hilar shadows may be slight or absent in the presence of compensatory emphysema

(7) Lateral roentgenograms are of particular value for the demonstration of changes in the position of the interlobar fissures In atelectasis of the upper lobe the major interlobar septum is displaced anteriorly At the same time the minor interlobar septum moves high up in the chest field Posterior displacement of the interlobar line is observed in lower lobe atelectasis Atelectasis of the middle lobe causes an approximation of the interlobar septa on the right side

(8) In massive atelectasis of one lung there is a dense homogeneous shadow over the entire hemithorax The heart and mediastinal structures are displaced toward the affected side The border of the heart adjacent to the atelectatic lung is obscured Similar but lesser displacement of the heart is noted in atelectasis of one of the lower lobes In upper lobe atelectasis a lateral shift of the trachea may be observed without change in the position of the heart Displacement of the mediastinal structures is absent when atelectasis of about the same extent and location occurs on both sides simultaneously

(9) Mediastinal herniation of the uninvolved lung is a sequel of atelectasis of the entire extent of one lung It varies in size from protrusion of the emphysematous lung just beyond the sternal border to an expansion to the lateral thoracic wall on the diseased side In the latter instance it is distinguishable from normal lung parenchyma by its greater radiotranslucency and by the extremely wide spacing of bronchovascular markings Moderate mediastinal herniation is recognized by its increased penetrability to x rays and by a vertical curved arch like delineation The convexity of the latter is toward the atelectatic lung Lateral roentgenograms are of value in the identification of pulmonary herniation

(10) Upward displacement of the hemidiaphragm is seen in atelectasis of one lung or of one of the lower lobes The shadow cast by the atelectatic lung is so dense that in the case of a right sided lesion no line of demarcation can be made out between the lung and the liver Artificial pneumoperitoneum is a safe and simple means for differential diagnosis in such instances In left sided massive atelectasis the position of the diaphragm can be easily determined by having the patient drink some soda water or barium suspension so as to outline the stomach Robbins and Hale pointed out that in some instances of lower lobe atelectasis of the chronic type the entire diaphragm is sharply outlined because the shrunken atelectatic lobe moves so far posteriorly and medially that the whole contour of the diaphragm is projected above the obscured portion of the lung Fluoroscopic examination is indispensable in such cases In many instances of chronic atelectasis of the lower lobes elevation of the hemidiaphragm cannot be demonstrated

(11) In some instances of atelectasis of the upper lobe the reduction in size of the latter may be so great that the lobe is hidden behind the mediastinal structures or the shadow cast by it may be misinterpreted as widening of the upper mediastinum

(12) Instillation of iodized contrast material (bronchogram) offers valuable help in diagnosis Roentgenograms taken in the standard oblique and lateral positions reveal either obstruction of the bronchus leading to the atelectatic region or bronchiectasis

(13) Fluctuations in the density of x ray shadows from day to day is often seen in atelectasis These changes are explainable

on the basis of alternating occlusion and reopening of the corresponding bronchus. Atelectasis regardless of its extent may clear spontaneously or by appropriate treatment.

(14) Complications such as pneumonia, abscess, pleural effusion are associated with corresponding changes in the roentgenogram. Tomograms may suggest the presence of bronchiectasis.

(15) Atelectasis of the lung in newborn infants shows certain characteristics which should be *mentioned*. When both lungs are extensively involved the thorax is cone shaped in contrast to the normal barrel shape. In addition to narrowing of the intercostal spaces there is an increased slanting of the ribs. Also there is a more or less homogeneous dense haziness over the lung fields. The appearance of atelectasis of one lung gives the same impression as one gains in adults. *Involvement of one lobe may be associated with scattered* mottling in other parts of the lung on the same side. Interestingly displacement of the mediastinal structures and rise of the corresponding hemidiaphragm in unilateral atelectasis are less pronounced in newborn infants than in adults. This may be attributable to the comparatively slight intrapleural negative pressure during the neonatal period of life.

Bronchoscopic examination may reveal the cause and type of bronchial occlusion. At the same time the bronchoscope serves as an indispensable therapeutic instrument.

TREATMENT

Relative to the problem of atelectasis two items are of utmost importance, namely prevention and adequate management of its underlying cause. When circumstances permit surgical intervention should be avoided in patients with acute respiratory infections. Appropriate selection and energetic administration of *specific chemotherapeutic agents* and antibiotics are mandatory for elimination of intercurrent infections of the air passageways. In chronic diseases of the lower respiratory tract deep breathing exercises or inhalation of a mixture of 5% carbon dioxide and 95% oxygen are of value in ridding the air passages from accumulated mucus. These measures are helpful in heavy smokers in whom one often finds chronic bronchitis with heavy tenacious bronchial exudate.

Mucus liquified by carbon dioxide is easily evacuated from the lung by postural drainage. When the patient is weak, debilitated or of advanced age this can be accomplished by elevating the foot of the bed by 15 to 18 inches. For patients whose general condition permits one can attain satisfactory postural drainage by positioning the patient so that *inflammatory* exudate finds its way into the major bronchi. The method advocated by Russo is serviceable. (1) In the knee chest position the kneeling patient stoops forward and is resting on his forearms with the palms outstretched. He remains in this position for 5 minutes and assumes the upright position while remaining on his knees. This maneuver is repeated several times until adequate bronchocatharsis is achieved. By rotating the trunk to the right or left lateral position and *remaining in this position* for a few minutes aids in the more thorough evacuation of the lung. (2) The patient may be seated on the edge of a low stool and assume the elbow-to-knee position. His knees are flexed, legs apart slightly more than the width of the shoulders and the trunk flexed as far down as possible while the elbows and forearms are in front of knees. (3) A similar maneuver may be carried out with the patient standing with lateral rotation of the thorax if necessary *for more* efficient drainage. Here again sufficient rest periods should be permitted so as to avoid undue fatigue. In instances where arthritis deformities of the pelvis or advanced age obviate the use of these methods Russo devised the crouching position which is done by resting with one forearm and hand on a chair while the opposite arm helps support the body on another chair and bending is far forward as *possible*.

The *ingenious studies* of Foster-Carter represent a significant advance in the appli

cation of postural drainage He emphasized the importance of accurately determining the segments of the lung involved and then positioning the patient so as to effect maximum drainage through bronchi connecting to these segments

The amount of preoperatively administered morphine should be reduced to the minimum Large doses of morphine may adversely affect the respiratory center cause bronchospasm interfere with normal bronchial peristalsis and ciliary function and also lead to inspissation of bronchial exudates Meperidin is a valuable substitute for morphine Its analgesic action is excellent It does not cause as much respiratory depression as morphine It leads to relaxation of the peribronchial smooth muscles When there is reason to assume that there is accumulation of mucopurulent material in the lung as in cases of chronic bronchitis bronchiectasis lung abscess infected cysts and other conditions it is expedient to resort to postural drainage or to encourage the patient to cough every hour so as to rid the lung of stagnating exudate In others it may be necessary to resort to bronchoscopic aspiration prior to major thoracic or abdominal operations The same intervention may be necessary during or immediately after operations In some instances satisfactory removal of mucus from the trachea and bronchi can be accomplished with a number *20–24 F* uretheral catheter

Scrupulous attention should be paid to the way abdominal binders are applied They should be placed so that the lower part of the chest is not covered and respiratory function *of the thorax and the diaphragm is not re*stricted

As soon as consciousness is regained after general anesthesia the patient should be encouraged to take deep breaths cough and expectorate After abdominal operations the nurse should support with one hand the abdominal wall and the site of the incision during coughing

Inhalation of a mixture of 5% carbon dioxide and 95% oxygen has been often found effective in cases where there was a reasonable suspicion or definite clinical evidence of postoperative atelectasis Following the pioneering observations of Henderson Scott and Cutler first used inhalations of carbon dioxide for the treatment of postoperative atelectasis Its efficacy in this respect is attributable to these factors (1) Carbon dioxide stimulates the respiratory center Consequently it induces increased respiratory excursions of the diaphragm and of the chest wall The ensuing amplified inspiratory expansion of the lung is associated with stretching and dilatation of the bronchial tubes and distentions of the alveoli (2) Carbon dioxide stimulates the peribronchial and peribronchiolar smooth muscles and leads to forceful peristalsis of the bronchi and bronchioles (3) Carbon dioxide liquifies mucopurulent inflammatory exudate by increase in the secretions of the mucosal glands of the lower air passages The apparatus used in practice consists of a cylinder which contains a mixture of 5% carbon dioxide and 95% oxygen A flow meter regulates the flow of gas per minute Inhalations are given through a face contour mask Five liters per minute are given to the patient for 15 minutes every 2 hours on the first day after operation and less frequently on subsequent days as required by the patient's pulmonary condition

There have been endeavors to utilize the beneficial influence of carbon dioxide by means other than by direct inhalations in the aforementioned form The method suggested by Duomarco and his collaborators in 1937 and the equipment devised by Harbord in 1939 have been superseded by the ingenious simple and practical procedure originated by Schwartz and his co workers in 1957 They *use a common black rubber tube with a* length of 125 cm and with an internal diameter of 3 2 cm When an individual inhales through a mouthpiece attached to this tube while his nostrils are pinched shut by fingers the physiological dead space of the lung is increased by 1 000 cc Breathing through this artificial dead space increases the pCO of the alveolar air and consequently the arterial pCO Rebreathing for 5 minutes every 2 hours was found effective by these clinicians for the prevention and treatment of postoperative atelectasis They recommend that in patients who are in a state of hypoxia a flow of

3 to 4 liters per minute of 100% oxygen be given into the distal end of the rebreathing tube. This treatment can be used in patients who are in coma. The mouthpiece is inserted between the lips and the nares are occluded by fingers of an attendant.

Inhalation of carbon dioxide by whatever means is contraindicated in patients with pulmonary hemorrhage, spontaneous pneumothorax, pseudohypertrophic emphysema, acute pleurisy and pronounced hypertension.

Bronchoscopic aspiration of tenacious mucus which occludes the lower respiratory passages is called for when inhalation of carbon dioxide and oxygen does not bring about the expected improvement in the patient's condition. With proper sedation and under adequate local anesthesia this procedure may be carried out repeatedly the same day or on successive days when the patient's condition so requires. Customarily bronchoscopy is performed in the operating room. However, bedside bronchoscopy may be safely carried out in patients who cannot be moved without serious complications or without danger to their lives.

Bronchoscopic intervention is of inestimable value in the treatment of atelectasis whether one is dealing with a postoperative condition or with one which develops as the result of bronchial occlusion due to aspirated foreign bodies and other conditions enumerated previously. Bronchoscopy gives an opportunity for direct inspection of the trachea and bronchi and thus it may reveal the exact type and extent of bronchial obliteration. Moreover immediate treatment of ulcers, granulation and benign tumors, also dilatation of stenosis are possible. Too, specimens removed bronchoscopically for biopsy permit the identification of the nature of the occluding tissue.

Auxiliary measures which may be helpful in the treatment of atelectasis are postural hyperventilation, thumping over the involved hemithorax, cocainization of the throat, administration of bronchospasmolytic drugs, liquefaction of tenacious pulmonary exudate, dislodgment of mucous plugs and inspissated inflammatory products from bronchi and bronchioles by mechanical means, aiding expectoration by relieving pain.

Sante first suggested rapidly turning the patient from side to side. In this manner it may be possible to ventilate occluded areas of the lung. By rolling the patient back and forth gravity may force some of the tenacious mucus from smaller bronchi to larger ones from where vigorous coughing may expell them. In some patients effective bronchial drainage is established by turning them from one side to the other side every hour. In others the type of surgical intervention permits placing the patient without causing pain in the knee chest position or to have the upper half of his body hanging down over the edge of the bed. He is kept in this position for 5 minutes. Frequent volitional coughing is mandatory during this period.

Sharp slapping on the back may reflexly induce more vigorous respiration or may mechanically dislodge obstructive mucus from the air passages and provoke coughing which is sufficient to rid the lung of the occluding exudate. For the purpose of this maneuver it is advantageous to have the patient lie on the side opposite to the atelectatic area. The upper part of the thorax should be lower than its base so as to utilize the force of gravity.

Cocainization of the throat was advocated by Grandstaff for the treatment of atelectasis. It has been shown experimentally that this maneuver causes a reflex relaxation of the peribronchial smooth muscles. In instances where it is reasonable to assume that spastic contraction of these muscles is responsible for bronchial occlusion and atelectasis it is likely to get favorable results from this treatment. Cocaine is used in a 5 to 10% solution. A cotton ball saturated with it is held in a curved applicator far back in the throat and into the pyriform sinuses. Similar effect may be expected from spraying the pharynx and hypopharynx with 4% solution of cocaine. Mention should be made in this connection of bronchospasmolytic drugs which can be given orally or by inhalation. Of the epinephrine like drugs isopropylarterenol has been found of superior value in my experience. It is available under a variety of proprietary names such as Isuprel, Aludrine, Norisodrine, Isonorin and I.P.A. Clopane hydrochloride is administered in combination with isopropyl arterenol, atropine sulphate and procaine hydrochloride

(Aerolon compound) Neosynephrine is chemically closely related to epinephrine An other effective bronchorelaxant is butanephrine Ephedrine and several ephedrine like chemicals are suitable for inducing satisfactory relaxation of spastic bronchi Of this group Orthoxine and Propadrine may be mentioned Theophylline with ethylenediamine is a remarkably efficacious bronchospasmolytic drug through its direct action upon the peribronchial smooth muscles My results with a number of anticholinergic preparations (parasympathetic blocking agents) have been highly satisfactory I prefer the administration of diethylmethylammonium bromide (Antrenyl bromide) The bronchospasmolytic action of prednisone and prednisolone is impressive indeed

Early rising and ambulation after major operations have substantially reduced the incidence of postoperative atelectasis It has been demonstrated that this routine promptly increased the tidal air the respiratory minute volume alveolar oxygen tension and the oxygen saturation of the blood

Liquefaction of thick viscous bronchopulmonary exudate may be attained by the administration of expectorants or by the inhalation of detergents or proteolytic enzymes Ammonium chloride is given in doses of 5 grains (0 3 gm) every 2 hours or every hour Potassium iodide loosens viscid mucopurulent exudates in the lower air passages by increasing secretions of the bronchial mucosal glands Also resorption of some of the exudates is accelerated Baker and his associates report clearing of postoperative atelectasis within 48 hours after intravenous injection of sodium iodide in from 1 to 2 gm doses twice daily For the prevention of atelectasis postoperatively they recommend the routine administration of one gram of sodium iodide intravenously twice a day for three to four days after major surgical interventions Adequate doses of ipecac may be helpful in the removal of sticky bronchial exudate Ipecac not only loosens adherent mucus by increased production of the mucosal glands but also it accelerates resorption of exudate and by effectively relieving bronchospasm it improves the peristaltic motion of the bronchi and thus aids in the self cleansing of the lung

Clearing of bronchial obstruction and consequent relief from atelectasis may be greatly facilitated by lysis of the occlusive inspissated material by inhalations of aerosolized trypsin Trypsin is the proteolytic enzyme of the pancreas Satisfactory results have been observed with the use of crystalline tryptar (Armour) It is dissolved in Sorensen's buffer solution so that three cubic centimeters of the latter contains 125 mg (125 000 units) of tryptar Some clinicians use a stronger solution namely 100 000 units per each cubic centimeter So as to avoid possible allergic side reactions it is well to give the patient 50 mg of diphenhydramine (benadryl) hydrochloride 30 minutes before treatment orally or subcutaneously The patient inhales the aerosolized solution from a nebulizer connected to an oxygen tank with a reducing valve set for a gas flow of 5 liters per minute Treatments are given three or four times a day and repeated daily for 2 or 3 days as circumstances demand One may add to the tryptar solution from 5 to 7 drops of isopropylarterenol in 1 200 solution Antibiotics are preferably administered separately It is expedient to interrupt the treatment when the patient is obliged to cough and expectorate and also in instances where tracheal aspiration is required for the removal of the liquefied mucus Special attachment is required when inhalations are given to patients with tracheotomy Peck and Levin reported on the effective use of tryptar by bronchoscopic instillation The patient is in the lateral recumbent position with the involved lung lowermost After bronchoscopic cleansing of the corresponding bronchial tract 5 cc of Sorensen's buffer solution containing from 125 to 250 mg (125 000–250 000 units) of tryptar are instilled into the bronchus of the involved lobe or lung After 1 hour in this position the patient is turned to the opposite side so as to aid expectoration of the liquefied material When necessary treatment is repeated once or twice at 2 or 3 day intervals In some instances more rapid relief is obtainable by bronchoscopic aspiration one hour after instillation of tryptar

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Triton A-20 is a wetting agent of proved

value for liquefying thick, tenacious exudate which blocks the lower air passages It is a 25% solution of Alevaire (Winthrop) The latter is a 0 125% aqueous solution of a detergent, Triton WR1339, in combination with sodium bicarbonate 2% and glycerin 5% Triton WR1339 is an oxyacetylated tertiary octyl-phenol-formaldehyde polymer Triton A-20 is available in liquid form in 500 cc containers It is given by inhalation through a nebulizer which delivers a fine mist Infants and children are placed in a plastic tent which covers the entire body Adults use a plastic tent which covers the head and the neck or take the inhalations through a face mask When high concentrations of oxygen are desirable, the nebulizer is attached to a suitable oxygen tank The oxygen flow from the tank is set at a rate of 8 liters per minute There is no need for bubbling it through a water bottle Adequate inhalation of oxygen can be secured by using a closed, ice cooled tent or a special oxygen aerosol tent On the first day, inhalations are given continuously for 10 to 12 hours, with interruptions only for cough and expectoration Subsequently, the solution is inhaled intermittently with a schedule of on 2 hours and off 2 hours three to four times during a 24 hour period, until complete recovery from atelectasis

Atelectasis caused by mucous plugs or by heavy, viscous exudate may be promptly relieved with the use of aerosolized inhalations of pancreatic desoxyribonuclease (dornase), an enzyme capable of liquefying thick, tenacious inflammatory products Armstrong and White first used it for this purpose Their favorable results have been corroborated subsequently by Salomon and his co workers, by Clifton and others One hundred thousand units of pancreatic dornase (Sharp Dohme) are dissolved in 2 cc of Sorensen's buffer solution or in physiological solution of sodium chloride and inhaled with a nebulizer connected to an oxygen tank The flow meter is set at 5 liters per minute Two treatments are given daily for a total of four Rarely, more than four treatments are necessary. There are only few, minor side effects

For the management of atelectasis in patients with postpoliomyelitic respiratory embarrassment a commendable routine was advocated by Camarata and his associates In non-tracheotomized patients they administer tryptar or Triton A-20 for facilitating the removal of occlusive exudate from the lung For this purpose a plastic tent, face mask or a nebulizer was used in the manner described previously For tracheotomized patients in a respirator they attached a vacuum cleaner machine to a porthole in the respirator and reduced the tank pressure to minus 40 cm of water. This negative pressure induces deep inspiration At this moment the bedpan port of the respirator is suddenly opened The ensuing rapid increase in pressure within the respirator causes the inhaled air to be expelled with great velocity The latter is sufficient to propel and suck the bronchial exudate through the tracheotomy opening They recommend 24 artificial coughs of this type to be given four times a day Also, it is suggested that for post poliomyelitic patients without tracheotomy, the attendant compress the thorax simultaneously with the expiratory phase of the respirator instead of using the vacuum machine.

To Barach and his associates belongs the credit for introducing cough machines for the removal of tenacious bronchopulmonary secretions Basically, their device produces cyclic inflation and deflation of the lung corresponding to the normal rate of respiration Inspiratory inflation of the lung is attained by a positive pressure of 30 to 40 mm of mercury At the peak of inspiration, the intrapulmonary air current is suddenly reversed and an outflow of great velocity is initiated by the application of negative pressure of 30 to 40 mm of mercury Lower pressures are used in children and infants The air inhaled under positive pressure dilates the bronchial tubes It is likely to penetrate to some of the unventilated and underventilated areas of the lung Also, it may mechanically detach tenacious exudate which is adherent to the mucosal surface Moreover, the rapid air current acts as an expulsive force (*vis a tergo*) during expiration It is indisputable, however, that the efficacy of this method is attributable chiefly to the expiratory blast exerted by the high velocity of air leaving the lung The

patient may expectorate spontaneously when the mucus dislodged from the alveoli and small bronchi (which have no cough reflex) reaches larger bronchi capable of initiating productive cough In cases where the cough mechanism is inadequate and the patient is unable to expectorate it is mandatory to aspirate the mucus from the trachea or pharynx

There are a number of acceptable cough machines available for hospital use

Equipment of this type should not be used for the treatment of atelectasis when the latter is brought about by factors other than accumulation of thick, viscid mucus in the lower respiratory tract For obvious reasons its use is contraindicated in patients with pulmonary hemorrhage and spontaneous pneumothorax

In patients with severe postoperative pain which interferes with clearing of pulmonary secretions after major abdominal or thoracic surgery intercostal nerve block may prevent or relieve atelectasis Since the first report of Gius on this procedure in 1940 its value has been confirmed by a number of clinicians

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CHAPTER 18

Cystic Disease of the Lungs

WILLIAM R FIFER M D

INTRODUCTION

THE FIRST report of cystic disease of the lungs is commonly stated to be that of Bartholinus in 1687 although Fontanus apparently described the condition in 1638 Laennec in 1819 discussed "cysts formed in the lungs and described the cyst as an accidental membrane forming a sort of shut sac commonly of roundish shape but sometimes irregular and anfractuous and containing a liquid or half liquid matter secreted by the membrane which encloses it"

In 1925 Koontz reported a case of congenital cystic disease in the *Bulletin of Johns Hopkins Hospital* and analyzed 180 cases gathered from the European literature This report in the American literature initiated widespread interest in the condition in this country Prior to Koontzs report the condition was only a pathologic curiosity while following his communication it become a clinical entity and was soon within the realm of surgically correctible conditions Bearing in mind that the first successful pneumonectomy was in 1933 and the first successful segmental resection in 1939 it is noteworthy that the first successful emergency resection of a tension cyst was performed in a 4 week old baby in 1943 (Fischer) Since pathological observations on these patients are now commonly made during life (at the time of surgery) and correlated with the course of the disease the clinical concept of cystic disease has broadened and become more complicated and classification almost impossible

CLASSIFICATION

The term cystic disease" of the lungs includes all air containing or fluid containing *spaces not caused by lung destruction* Increasing knowledge of this group of diseases has not only failed to simplify diagnosis but it has confused rather than clarified classification The arguments concerning congenital versus acquired etiology still prevail in the current literature and various classifications are based on such things as (1) the contents of the cyst (whether fluid air pus blood or combinations of these) (2) the presence or absence of bronchial communication and (3) the presence or absence of an epithelial lining One must also decide whether such conditions as cystic bronchiectasis and acquired pulmonary cavitations (such as those due to tuberculosis cavitating carcinoma lung abscess etc) *should properly be included in* the classification of cystic disease To further confuse the issue cysts are classified as single multiple or diffusely situated (honeycomb lung) and the inclusion of pulmonary blebs and bullae into the classification leads one inevitably into the realm of pulmonary emphysema which does not properly belong in this chapter

It is useful however to review some of the various attempts at classification of cystic disease to better understand the embryology and pathophysiology of these conditions and to help relate those which seem diverse

DEVELOPMENT ANATOMY AS A BASIS FOR CLASSIFICATION

The embryology of the lung is reviewed by those who choose to classify cystic disease into congenital versus acquired Development of the lung begins in the three to five week embryo[15,38] with the division of the foregut into a ventral or tracheal bud and a dorsal or esophogeal bud Any tissue displaced at this time may develop either into the so called "true bronchogenic" or into esophageal (or gastric) cysts found in the mediastinum or at the lung hilus in adult life[23] which are present as solid rather than air-filled structures The tracheal bud undergoes progressive growth, elongation and branching to form the bronchial tree and alveoli During this developmental process, any sequestration of bronchial tissue or abnormal diverticulation provides the basic alteration from which cyst formation later evolves[21] After the cystic structure is formed it may be completely sequestered from the tracheobronchial network, may remain connected by a fibrous cord, or may have a persistent bronchial communication,[26] and thus be aircontaining In such lesions as true bronchopulmonary sequestration, cystic hamartomas or bronchial cysts misplaced into the mediastinum, the "congenital' theory of development seems most tenable

Another point which is stressed by those writing of congenital" cystic disease is that the development of the lung is not complete at birth hence it is not possible to assume that all post natal cystic disease is of necessity "acquired' The older view of Koelicker that an infant is born with both lungs completely formed and that, following birth only growth of the preformed elements occurs, has been disproved by the work of Broman, Willson Bremen Meyer and others[37] who have demonstrated that there is continuing post natal development of the bronchopulmonary tree by actual increase in the number of lobules, rather than simple increase in size of preformed elements Thus King[15] states that lung development is not complete until age 15

It seems best to assume that in many cases of cystic disease the pathogenesis cannot be definitely determined Some cysts are surely congenital' in origin, while others are "acquired" usually as a result of pulmonary infection which produces a check valve bronchostenosis In still other situations acquired factors probably cause cystic disease by distortion of the developmental process[37]

PATHOLOGY AS A BASIS FOR CLASSIFICATION

Cystic disease has been classified according to histologic criteria into two broad types of cysts, bronchogenic and alveolar This classification rests on whether bronchial (columnar) or alveolar (flat squamous) epithelium lines the cyst, and some[27] contend that the "bronchogenic" cysts are congenital, while the "alveolar are acquired Others have stressed that the presence of an epithelial lining identifies a cyst, while a bulla has no epithelial lining Belcher[12] points out, however, that the presence or nature of an epithelial lining is not diagnostic since such lining may be flattened from columnar to cuboidal by pressure, undergo squamous metaplasia or be destroyed by infection, while on the other hand abscesses, (which result from infectious necrosis of lung parenchyma) or infected bullae may become lined by epithelium especially if externally drained[17] The histologic appearance of the cyst wall is considered more important than the lining by many[14] who contend that an acquired' cyst will have an orderly arrangement of elements in the wall exactly like a normal bronchus, while "congenital' cysts walls will likely contain disarranged cartilagenous and muscular elements as well as fibrous tissue and glandular remnants It seems obvious that the histopathology described at the time of surgery or necropsy may be considerably altered (by the occurrence of infection etc) from that which originally existed

CLINICAL FACTORS AS A BASIS FOR CLASSIFICATION

Since the advent of thoracic surgical correction of cystic disease there has been a tendency to disregard the theoretical classification

in favor of a practical therapeutic approach Many surgeons have said "it does not matter nor can we determine, whether cystic disease is congenital or acquired—what does matter is that a given cystic lesion is or is not, amenable to surgical removal" This has led to a more gross, surgical pathologic classification such as whether the cystic area is or is not connected to the bronchial airway, or whether there is or is not an aberrant arterial supply (see intralobar bronchopulmonary sequestration) The clinician has asked "What is the pathologic physiology of this cyst in terms of pulmonary function studies?" and "how much associated emphysema is present?" One desires to know whether infection, overinflation, or spontaneous pneumothorax is likely to complicate a given cystic lesion

In keeping with the surgical era of thoracic disease then, we have chosen to classify cystic disease into workable clinical categories which will later be discussed in order

TABLE I

CLASSIFICATION

I Problems in Cystic Disease of Infancy
- A Tension cysts
- B Post infectious pneumatocele
- C Congenital lobar emphysema

II Problems in Infected Cystic Disease
- A Cystic bronchiectasis
- B Infected bronchogenic cysts
- C Lung sequestrations

III Problems in Adult Non infected Disease
- A Cystic disease associated with more or less pulmonary emphysema
- B Localized pulmonary cysts discovered on x ray surveys

IV Problems of "Specific" Cystic Disease
- A Associated with specific infections
- B Cystic disease associated with systemic diseases
- C Miscellaneous

PROBLEMS IN CYSTIC DISEASE OF INFANCY

TENSION CYSTS

The problem of tension cysts of infants is being more commonly recognized today This condition presents as an acute emergency because the infant rapidly becomes cyanotic and dyspneic due to displacement of normal lung by the rapidly expanding, tensile cyst The mechanism of formation is partial bronchial occlusion of the ball valve variety, permitting air to enter but not leave the cyst (see Fig 1) The cause of bronchial occlusion is thought to be most often infectious, with resultant increased thick bronchial secretions, and edema, which impede egress of air through the tiny bronchus, although it is not usually possible to delineate the exact mechanism Some check valves may be due to abnormal development of bronchial walls or linings

In any event the disorder appears in the neonatal period, commonly and presents a definite hazard to life Upon discovery of the dyspneic, cyanotic infant with physical findings not unlike those of a pneumothorax, an immediate emergency chest x ray should be performed This will disclose in case of a tension cyst, a large radiolucent area filling a whole lobe or an entire hemi thorax, and displacing the heart and mediastinal structures to the opposite side (see Fig 2) A valuable differential point between a tension cyst and a pneumothorax is that, in the latter, the amorphous radiodense mass of collapsed lung will usually be seen lying in the perihilar region on the involved side Having diagnosed the condition, emergency thoracotomy with resection of the cyst is necessary to save life [18] While waiting for the surgeon, the house officer administers oxygen and remains constantly at the infant's side with syringe and needle in readiness since aspiration of some of the air under tension may be a life saving temporary procedure [11 18] Successful surgical removal has been accomplished on infants as young as 5 days,[22] and as small as 1900 gm

POST INFECTIOUS PNEUMATOCELES

Caffey[20] has emphasized an important group of infants and children, previously mentioned by Pierce and Dirkse[32] in whom pneumatoceles (Gr air tumor) develop in the waning stages of an acute respiratory infection Caffey's contribution was his demonstration that most

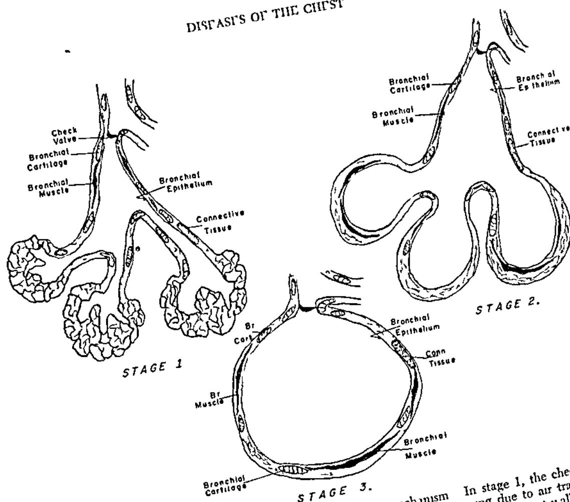


Fig 1 Development of a cyst due to a check-valve mechanism In stage 1, the check valve is shown in the terminal bronchiole Stage 2 portrays progressive ballooning due to air trapping, and Stage 3 shows the fully developed cyst Note how the various components of the cyst wall (bronchial cartilage, muscle, and connective tissue) become displaced from their natural relationship as progressive dilation occurs Caffey feels that this displacement occurs in these acquired lesions and refutes the validity of displacement as a criterion of their "congenital" origin (Modified from Caffey *Pediatrics*, 11 61, 1953)

of these cystic lesions will regress spontaneously in time This group of patients develops the pneumatocele due to bronchial infection with exudate and edema producing a check-valve mechanism, often occurring during the course of pneumonia caused by M pyogenes (staphylococcus) an infection which is commonest in the first year of life These cases are discovered when, as the child is recovering from his pneumonia, the x ray begins to show "soap bubble" radiolucencies (see Fig 3) in the previously consolidated area[29] The subsequent x rays which show clearing of the pneumonia reveal, in its place, a large cystic lesion The cystic area then must be differentiated from an abscess cavity or a "congenital" cyst which has become infected[29] Although roentgenographic differentiation is not always possible, the radiologic appearance is often helpful in the differentiation A pneumatocele has a paper thin wall, while abscess cavities or infected cysts have thick walls Also the size of pneumatoceles may fluctuate rapidly, and they may suddenly disappear The clinical appearance of the child, who by this time will be afebrile and clinically much improved, will also help diagnose the lesion as a pneumatocele This clinical well being will also permit continued conservative management in the anticipation that the lesion will regress spontaneously, as noted by Caffey This regression may take weeks or months, but



Fig. 2. Anteroposterior and lateral views of a tension cyst in an infant. Note displacement of mediastinum by enlarging cyst in AP view and clearly identifiable cyst wall in lateral view. (From Swan: *Pediatrics 14*:651, 1954.)

the waiting is rewarded by the avoidance of surgery. In those that do not regress after several months resection should be considered because of the threat of repeated infection of the cystic area.*

It should not be concluded that this group of post-infectious pneumatoceles will always be as easily recognized as the classical sequence of events described above. When one is presented with a child whose x-ray reveals a cystic lesion he must rely on multiple diagnostic aids to delineate this group. A careful history of previous respiratory illness will be helpful, for a cyst found in the absence of such history may be truly congenital in origin. Securing all previous x-rays is also important to retrace the characteristic chain of events described herein which leads to a post-infectious pneumatocele. Careful clinical interpretation of the situation may be rewarded by the spontaneous regression of the lesion without surgical intervention.

CONGENITAL LOBAR EMPHYSEMA

This clinical entity, which occurs in infants and young children, is defined as cystic or bullous overexpansion of an area of lung, usually a lobe, with resulting compression of the adjacent normal lung, often to the point where the hyperinflated lobe fills the entire hemithorax. Overstreet (1939) first discussed this condition but he cited a case described by Peeler and Philips in 1922. The clinical situa-

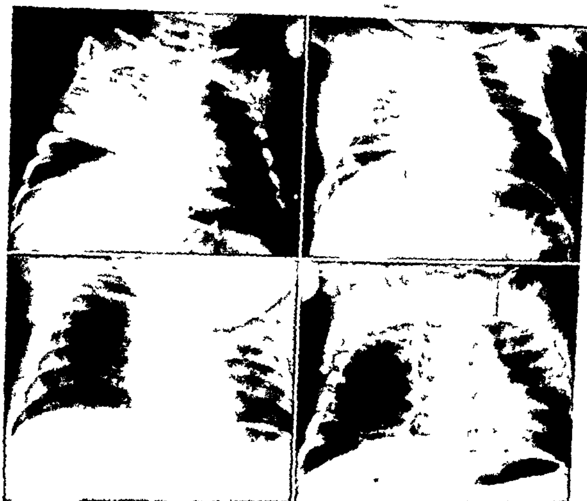


Fig 3 Anteroposterior roentgenograms of an infant showing (a) pneumonic consolidation progressing (b) to "soap bubble radiolucencies within the area of consolidation and further (c d) to an enlarging post infectious pneumatocele (From Campbell *Am J Surg* 89 1013 1955)

tion develops less acutely than the tension cyst category of infants but may eventually lead to dyspnea and cyanosis It is designated "congenital lobar emphysema" (a poor term) because the condition is most commonly caused by a congenital absence of bronchial cartilage rings practically always in the upper lobe thus allowing the opposing bronchial walls to fall together during expiration another example of a check valve mechanism Because air is able to enter the lobe but is prevented from leaving progressive expansion under tension occurs with resulting compression of adjacent lung

Other causes of the bronchial obstruction have been cited by Jewsbury[3] as causative of this condition valve like folds of the bronchial mucosa kinking of the lobar bronchus abnormal vessels which compress the soft bronchus (such as patent ductus arteriosus) foreign bodies and thick secretions Occasionally no cause is found either at surgery or in studying the resected specimen It is not clear why faulty cartilage development the most common cause is limited to one lobe alone and the term is a poor one because

[illegible]

that two conditions are necessary to produce lobar emphysema first the bronchial check valve mechanism and second inflammatory occlusion of the pores of Cohn which normally



Fig 4 Anteroposterior roentgenograms of an infant illustrating congenital lobar emphysema" of the left upper lobe (a) before resection and (b) postoperatively (From Campbell *Am J Surg* 89 1015 1955)

allow interchange of respiratory gases between adjacent respiratory units (so-called collateral air drift)

Radiographically it is often difficult to distinguish congenital lobar emphysema from a tension cyst (see Fig 4) as they differ only in anatomic distribution All cases should be considered for thoracotomy to remove the tensely emphysematous lobe thus permitting the normal lung to re expand At surgery one sees an extremely distended lobe which fails to collapse when the pleural space is entered[4] Following successful lobectomy the prognosis for normal health growth and development is excellent

PROBLEMS IN INFECTED CYSTIC DISEASE

CYSTIC BRONCHIECTASIS

There has been discussion as to whether cystic bronchiectasis is an "acquired" lesion in the sense that it is the result of bronchopulmonary suppuration early in life or whether it is "congenital" in the sense that it is results from faulty budding of the embryonic bronchial tree resulting in the malformed cul de sacs seen as a "bunch of grapes" on the bronchogram If the latter hypothesis be accepted one can accept a continuum of developmental defects ranging from the single "true congenital cyst" lined by bronchial epithelium and usually not in communication with the bronchial tree to the multiple sacs of cystic bronchiectasis involving a segment a lobe or a whole lung which is in free communication with the bronchial tree In either case infection sooner or later dominates the clinical setting Some authors[4] argue that the upper lobe location or the fact that all the cysts are about the same size differentiate "congenital" bronchiectasis from the usual variety and the occasional finding of an aberrant artery to a sequestered area of cystic bronchiectasis increases the tendency to consider the complex to be congenital" (developmental) in origin



Fig 5 Infected bronchogenic cyst Figure (a) shows the roentgen appearance of the lesion and figure (b) is a photograph of the resected specimen (From Moersch *J Thoracic Surg* 16 184 1947)

It seems obvious that many writers do not clearly distinguish between solitary or multiple round cysts and the lesser degrees of dilatation which are now called bronchiectasis We now consider bronchiectasis an almost entirely acquired condition and it would not bear mention in this chapter were it not for the terms congenital and cystic which are often applied to uncommon cases

The subject of bronchiectasis is considered fully in another chapter

INFECTED BRONCHOGENIC CYSTS

This subject is included in the section on infected cystic disease because most solitary true bronchogenic cysts first become clinically manifest because of infection within them These cysts are lined with columnar bronchial epithelium (unless the lining is modified by infection) and 20% [6] or more are connected to the bronchial tree so present an air fluid level on radiographs They are of ovoid shape vary from 1 to 9 cm in diameter and the wall is 2 to 4 mm thick The wall of these true cysts as mentioned above consists of fibrous tissue and smooth muscle containing islands of cartilage nerves and blood vessels in disarray (see Fig 5)

The usual clinical story sounds like pneumonia from which the patient recovers with therapy but the round pulmonary density persists If it drains adequately into a bronchus the patient coughs up large quantities of thick purulent (sometimes putrid) material leaving the x ray picture of a thick walled excavation with an air fluid level It is then difficult to determine whether one is dealing with an abscess cavity or an infected lung cyst From the practical standpoint the clinical management is the same The essentials of therapy are drainage antibiotics both systemically and by aerosol and supportive care *One is more tempted to resect an infected cyst than he is an abscess cavity* because the likelihood of reinfection of the former is greater The expected finding at thoracotomy is that the rest of the lung is entirely normal and after resection of the optimal area of lung (wedge segment or lobe) necessary to remove the cyst no further cystic disease is anticipated in these patients These solitary true cysts are too limited in area to interfere with pulmonary function and too

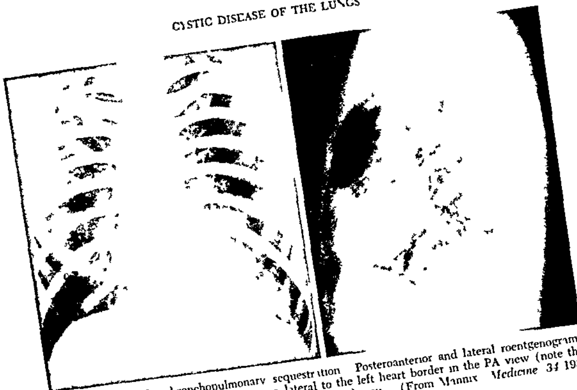


Fig 6 Intralobar bronchopulmonary sequestration. Posteroanterior and lateral roentgenograms show the sequestered mass of cystic tissue lateral to the left heart border in the PA view (note the air fluid level) and in the posterior gutter on the lateral view. (From Mannix *Medicine* 34 193 1955.)

thick walled to distend into "balloon" cysts (in general) so their only threat is infection.

LUNG SEQUESTRATIONS

This problem is considered here because the sequestered area consists of single or multiple cyst like spaces which are infected. It differs from cystic bronchiectasis or infected bronchogenic cyst in that the arterial blood supply is derived from the systemic circuit. In fact, Johnson[4] has called bronchogenic cysts "sequestered lung without the aberrant blood supply."

Varieties of this condition were described as early as 1777 by Huber[5] and have been divided into "extralobar sequestrations" (superior or inferior mediastinal accessory lung) which are simply variants of bronchogenic cysts which derive their arterial supply from either the bronchial arteries or thoracic aorta and "intralobar sequestrations" in which the cystic aberrant vessel complex is contained within a single lobe. Pryce[11] first called the condition "intralobar bronchopulmonary sequestration" in 1947 and described the embryogenesis. "A persistent artery from the dorsal aorta instead of the ventral aorta to the pulmonary anlage attaches itself to one of the bulbous growing tips of the budding bronchi and then enters into competition with the developing pulmonary artery. As the embryo grows and straightens and as the lung shifts to a more cephalad position the captive bulb is gradually torn away and isolated (sequestered) producing nests from which cysts may develop."

The sequestered segment may rarely be simply bronchiectatic lung tissue but more often is a system of branching bronchi one or more bronchogenic cysts or a polycystic mass. One or more of the cyst like spaces usually communicates with the rest of the bronchial tree so the x-ray appearance is often a dense mass with multiple fluid levels (see Fig 6). The aberrant artery consists of one to four vessels most commonly arising from the descending thoracic aorta[8] invested in the pulmonary ligament. More of the arteries are histologically pulmonary in type (elastic) rather than systemic (muscular) so

there is danger of avulsing them with fatal hemorrhage at the time of surgery. The venous drainage is usually quite normal. The sequestered portion is usually within the lower lobe, somewhat more commonly on the left than on the right, and may be discovered purely by routine roentgenography or by the clinical condition associated with infection and purulent sputum production from the cyst like mass. The diagnosis should be suspected from the x-ray, and resection should be carried out, bearing in mind the hazard of hemorrhage from the aberrant blood supply. The sequestered area may appear pink in color at thoracotomy, (because of the absence of anthracotic pigment in cases with no bronchial communication) a handy warning to the surgeon to beware aberrant vessels.[2]

Diagnostic efforts may be hampered by the facts that bronchoscopy is often not helpful, and the sequestered cystic mass may not fill bronchographically. Correct diagnosis will be rewarded by safe removal of abnormal tissue susceptible to repeated infections.

PROBLEMS IN ADULT, NON-INFECTED CRYSTIC DISEASE

CYSTIC DISEASE ASSOCIATED WITH MORE OR LESS PULMONARY EMPHYSEMA

This group of patients with cystic disease present themselves to the physician because of complaints referrable to the presence of some degree of pulmonary emphysema (dyspnea, *cough and wheeze*). *The cystic disease is of* the "balloon" type—that is, alveolar rather than bronchogenic. These "alveolar cysts" are thin walled, lined by flattened squamous epithelium, and cause trouble because of their tendency to expand rather than become infected (unlike bronchogenic cysts, which rarely undergo expansion but commonly become infected). These cystic areas develop because *of ball-valve bronchiolar narrowing in the more* distal reaches of the bronchial tree, due to tenacious secretions, bronchiolar suppuration and edema. Their interference with lung function depends upon the size they attain, with resulting compression of adjacent functioning lung tissue. They are closely grouped with (and hard to differentiate from) the more common blebs and bullae associated with *pulmonary emphysema*. Some authors[1] prefer the term air cyst to embrace the entire group of pulmonary air containing spaces, and discard the old terms bleb, bulla, pneumatocele, aerogenous cyst, balloon cyst, tension cyst, etc. Still it seems useful, because of their frequent produced by rupture of surface alveoli into the space beneath the visceral pleura. Blebs vary from tiny surface hemispheres too minute to be detected by roentgenograph to large, easily visible peripheral radiolucencies which lack lung markings. They grow because of check-valve arrangement, and rupture frequently, producing *spontaneous pneumothorax*. They are usually associated with diffuse, vesicular emphysema at the autopsy table,[13] yet their clinical manifestation (spontaneous pneumo-

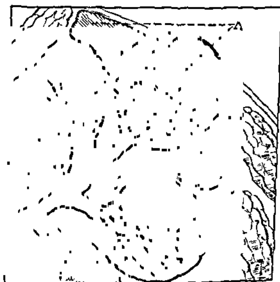


Fig 7. The formation of a subpleural bleb is shown in "A" above. It is to be distinguished *from a bulla, found within the substance of the* lung, and illustrated in 'B' above. (From Woods, *J Internat Coll Surg*, *19*:569, 1953.)

thorax) is primarily a disease of college age persons while emphysema is an old man's disease

A bulla (see Fig 7) is an air sac deeper within the lung parenchyma produced by the breakdown of interalveolar septa resulting in an air space whose walls are formed by ragged adjacent lung tissue an end result of severe vesicular emphysema (dilatation of alveoli associated with loss of pulmonary elasticity)[4]

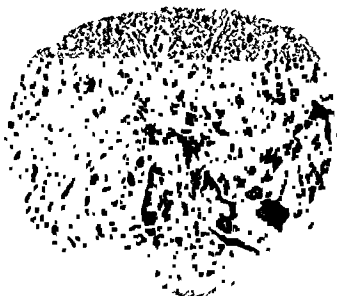
From the clinical standpoint alveolar cysts blebs and bullae are often combined with various degrees of emphysema and exact differentiation cannot be made radiographically or pathologically[30] As a practical matter they are simply various expressions of the same fundamental pathologic physiology These expressions form a clinical spectrum of disease varying from diffuse vesicular emphysema involving to the same degree every square inch of lung through various amounts of localized cystic disease in a basically emphysematous lung (bullous emphysema) to sharply localized cystic disease compressing large areas of otherwise fairly healthy lung Each patient must be evaluated individually seeking to answer the question Is the cystic disease sufficiently localized so that resection of the cystic areas will permit compressed more normal areas to expand and improve function? Or are the cystic areas insufficient to explain the poor ventilation of a basically emphysematous lung? Surgical opinion varies from those who believe that most patients with emphysema deserve exploration with resection of all grossly cystic areas to those who will remove only the expanding giant cysts of a so called vanishing lung"[12] to permit escape of compressed adjacent units It is generally concluded that resection is the only indicated therapy today as needling is dangerous and Monaldi suction produces variable results The question simply is—which patient will benefit by surgery?—and as stated above each case must be decided on its individual merits The patient with a symptomatic giant air cyst whose symptoms are exactly like those of pulmonary emphysema can actually be restored to useful function by cystectomy[7] so we must be continually watchful for him The patient whose symptoms are truly due to diffuse emphysema however and whose lung incidentally bears some



Fig 6 Echinococcus cyst of the lung (From Evans *Radiology* 1943)



Fig 9 Figure A above shows the radiologic appearance of honeycomb lungs during *spontaneous* pneumothorax Figure B below shows a photograph of a cut section of lung showing the uniform distribution of the cysts in honeycomb lungs"



cystic areas may be immeasurably harmed by ill advised surgical intervention How useful pulmonary function studies will be in the critical evaluation of these cases is not yet known[18] These studies are seriously limited in usefulness because of the function of the cystic area cannot be separated from that of the adjacent lung and the potential function in the compressed lung (recoverable by surgery) cannot be measured beforehand It is obvious that any surgeon's success in this difficult field rests upon his selection of cases and upon maximal preservation of normally functioning lung tissue

LOCALIZED PULMONARY CYSTS DISCOVERED ON ROUTINE ROENTGEN SURVEYS

Occasionally an asymptomatic patient is found to have a localized cyst or group of cystic lesions by routine roentgenogram If no bronchial obstruction can be demonstrated by the usual methods (bronchoscopy and bronchography) it seems adequate to simply follow the patient periodically If the cyst is seen to grow progressively in size or if symptoms (dyspnea etc) develop resection is indicated

PROBLEMS OF "SPECIFIC" CYSTIC DISEASE

CYSTIC DISEASE ASSOCIATED WITH SPECIFIC INFECTIONS

This is a group of patients in whom cystic lesions develop in the course of certain specific infections These lesions include the well known "tension cyst" seen in exudative pulmonary tuberculosis which is produced by a temporary bronchial check valve due to tuberculous endobronchitis The lesion must be differentiated from cavity formation, which it superficially resembles since it possesses wholly different implications Another specific infection which commonly causes a cystic lesion (or is a thin walled cavity?) is coccidioidomycosis (see chapter on pulmonary mycoses)

Cysticercosis and hydatid disease (echinococcus cysts) are other specific infections which cause cyst formation The latter is a common cause of chest pain cough and hemoptysis in sheep raising countries such as Australia and New Zealand where it has been shown that 23% of the hydatid cysts are located in the lung[33] (see Fig 8)

CYSTIC DISEASE ASSOCIATED WITH SYSTEMIC DISEASES

In the group of diseases now classified as histiocytosis" (Letterer Siwe Hand Schuller Christian and eosinophilic granuloma) the chest x ray often reveals diffuse cystic changes (see Fig 9) referred to as "honeycomb lungs [30] It appears that these cystic lesions result from necrosis in nodules of histiocytic tissue (diffuse nodularity in the lungs is not rare in histiocytosis) [9]

Cystic lungs have also been reported in tuberous sclerosis [?] and in pituitary and hepatic disease[31] (polycystic disease)

MISCELLANEOUS

In closing it should be mentioned that diffuse tension cysts have been seen in association with pneumonia due to volatile oil inhalation (kerosene) which produces an irritative bronchiolitis with resultant check valve mechanism [15]

Also described are "post traumatic" cysts which are localized collections of air (pneumatoceles) in the lung parenchyma caused by rupture of small bronchi due to chest trauma [19] These usually disappear spontaneously

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CHAPTER 19

Tumors of the Chest

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TUMORS of the chest present a very interesting and at times very puzzling group of conditions which may tax to the very limit the diagnostic and therapeutic acumen of even the most experienced physician. Virtually an unknown field except for tumors of the chest wall prior to the days of x-ray studies of the chest, it increased very rapidly as x-ray studies of the chest in the Public Health Surveys revealed many hitherto unsuspected and clinically unrecognized conditions. There are no accurate figures on the exact incidence of chest tumors in the general population, but certain studies of large groups of individuals have revealed approximately 2 tumors per 5000 films made.

Chest tumors, exclusive of those arising from breast, skin and subcutaneous tissues, may for purposes of description be considered under tumors of the chest wall, tumors of the mediastinum and diaphragm, and tumors of the lung. Within each category they may be divided into benign, primary malignant, metastatic tumors and inflammatory masses which may be confused with tumors. Because of the wide variety of structures normally within the chest, a great variety of masses may be encountered, some of them commonly, others infrequently and many very rarely. Some may be easily recognized, others require considerable study for their proper evaluation, while still others defy any accurate clinical or preoperative diagnosis and may even baffle the pathologist after their removal when all local relationship and site of origin are accurately known.

MODE OF DISCOVERY

While some thoracic tumors present themselves exteriorly and hence are easily recognized as such, the majority are deeply placed and do not come to the patient's attention. Some thoracic tumors produce symptoms for which the patient seeks relief and which will direct attention to a local tissue or organ for study as to the possible cause of the trouble. Many, however, produce no such localizing signs and are found only by careful study, while many more are completely silent and hidden and are discovered accidentally or at least unexpectedly in the course of examination, oftentimes while searching for other things. Routine x-ray studies, either on community-wide surveys or on routine hospital admission, have brought to light thousands of chest tumors completely unsuspected by the individual or his clinician.

HISTORY

The history of the patient with a chest tumor may be significant, especially in the patient who has discovered a "lump" himself or one who has chest pain, tightness, shortness of breath, dysphagia, cough, expectoration, hemoptysis, wheezing, orthopnea or cardiac disturbance. It may serve to direct the physician's attention to a certain intrathoracic organ or structure for an explanation of the symptom. On the other hand, probably the majority of tumors, even including some of large size, produce few or no symptoms to attract the physician's attention to it. Many may remain completely silent for long periods of time, even when known to exist. History taking should include questions relative to function or malfunction of the organs normally resident within the chest and those which

traverse it, and even to some of its close neighbors such as thyroid, stomach, colon, which may invade the chest but are not normally resident therein

A history of distant organs and past happenings may also be important in determining the nature of an intrathoracic mass A past history of trauma may explain the presence of the spleen, omentum, stomach, colon, small intestine or liver within the thoracic cage A previous history of goiter or a thyroid operation may give the clue which leads to the recognition of a displaced or intruding substernal thyroid A history of urinary or gastrointestinal bleeding may lead to the discovery of a malignant tumor in the urinary tract colon or stomach with metastatic extension, perhaps presenting as a chest tumor A history of joint trouble, a draining sinus or urinary symptoms may give the clue to the recognition of a tuberculous process which may also be the cause of the questionable chest lesion The history must be complete and extensive as all good histories should be It may well pay off for the time and care spent upon it

PHYSICAL EXAMINATION

Inpection

Tumors of the chest wall bulging outwards may be visible on simple inspection Tumors of the ribs and sternum and also cartilages, scapulae and clavicles usually present in this way, as do ulcerating abscesses of empyema, suppurating parasternal nodes, osteomyelitis and so forth, whereas many tumors of the ribs, cartilage and intercostal nerves only rarely present externally Any tumor in the chest locally or unilaterally may alter respiration, rib or diaphragmatic motion, cause bulging, retraction or pulsation in intercostal spaces, and change the general contour of the chest to give visible evidence of its presence Many such alterations are significant

Palpation

Careful palpation of the chest may reveal many findings of diagnostic importance Muscle spasm, muscle atrophy, local induration or softening, local temperature changes, change in excursion or mobility, presence of normal or abnormal pulsations, alterations in tactile fremitus, palpable vibrations or thrills, may all have diagnostic significance.

Percussion

Percussion of the chest and its contents by direct and indirect techniques is still a valuable method of examination, in outlining organs and abnormal masses Alteration in resonance or tympany, impaired resonance, dullness, flatness, may help to establish the diagnosis without special studies

Auscultation

The stethoscope still is a valuable diagnostic instrument, when duly appreciated and utilized by the examiner Too commonly, it is totally discarded and complete reliance placed upon the laboratory studies to make or confirm the diagnosis Alterations in the heart tones, their character and positions, the presence of murmurs or bruits, alteration in breath sounds from normal to distant or their absence in local areas, amphoric transmission, the presence of a local wheeze or rhonchus, may be of great aid Alteration in these findings may indicate emphysema, pneumothorax, pleural effusion, consolidations of various types and bronchial obstructions and compressions, and may give the clues which establish the diagnosis Auscultation of the abdomen as well as the chest should be important and familiarity with it more so The recognition of bowel sounds in the chest in diaphragmatic hernias, both traumatic and congenital, and the recognition of a perisplenic friction rub as distinguished from a pleural friction rub, may be of value to the clinician

General Physical Examination

The making of a complete physical examination is always important, but especially so in the study of a patient presenting some bizarre condition within the chest Many comparatively simple things at a distance from the thorax may give the clue which establishes the diagnosis of the condition within the chest. Headache, swallowing difficulty, or the eye signs of a cerebral lesion may point to a cerebral metastasis from carcinoma of the lung Alteration in voice and phonation may call

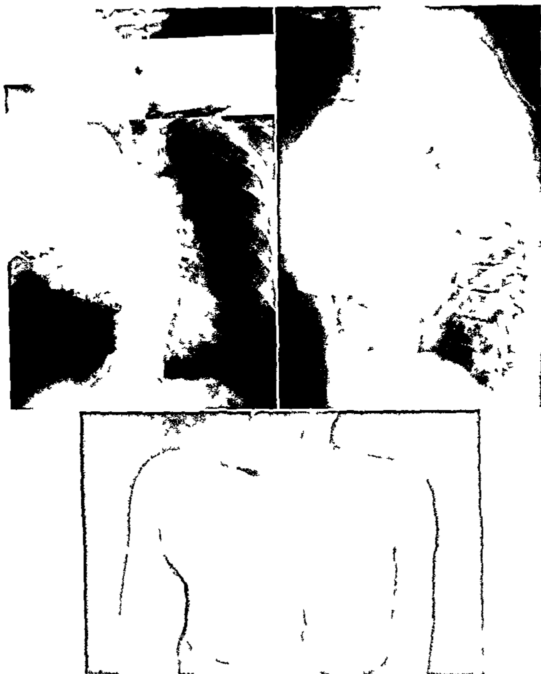


Plate 1 Osteochondroma of Chest Wall M O female age 65

Fig 1 and 2 Huge tumor showing extent of tumor within chest
Fig 3 Photo Huge external mass of tumor History of tumor for 40 years

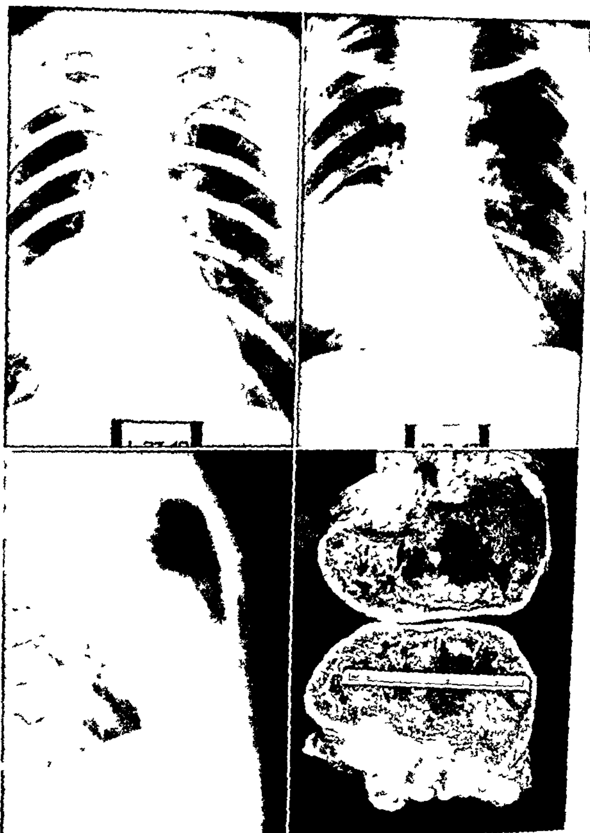


Plate 2 Chondrosarcoma of Rib E B male age 45

Fig 1 1 27 40

Fig 1 Speci

Reconstruct on w th fascia
9 years later







Plate 3 Osteochondrosarcoma of Rib W Q male age 37

Fig 1 and 2 Tumor of left anterior third rib resected 10 10 47
Fig 3 Specimen Patient died [illegible] recurrence December 1950

attention to a vocal cord paralysis secondary to bronchogenic carcinoma, substernal thyroid or other malignancy within the chest The eye changes of a Horner's syndrome, lack of sweating, difference in color of the two sides of the face may call attention to a sympathetic nerve trunk interruption by bronchogenic carcinoma, lymphoma, aneurysm, or neurogenic tumor Changes in the neck, axilla, or groin may give evidence of leukemia or Hodgkin's disease to explain other masses within the chest The finding of an abdominal or pelvic mass may point to an abdominal primary malignancy with metastasis appearing in the chest as an isolated tumor Pelvic examination may reveal a local tumor to explain an otherwise mysterious pleural effusion (Meig's syndrome) Alteration in reflexes or knee jerks may call attention to central nervous system lues to suggest that an intrathoracic mass may be an aneurysm Innumerable such examples could be cited, all of which emphasize the importance of a complete and thorough physical examination on all patients, even though all interest and information seems to point exclusively toward the thoracic cage

SPECIAL EXAMINATIONS

X-ray

Probably the single most important examination for the recognition and diagnosis of thoracic tumors is the roentgen-ray examination of the chest For screening purposes, a single 14 by 17 inch x ray picture of the chest will reveal the majority of thoracic tumors, even though an occasional tumor such as a small mediastinal dermoid or teratoma, a small thymic tumor or an occasional carcinoma may be hidden by the cardiac shadow or be lost in the mediastinum The small 70 mm, or slightly larger film, will usually reveal the larger thoracic tumors but may not show some of the smaller tumor masses *Stereoscopic* 14 by 17 inch films of the chest are of distinct value in certain situations but do not as a rule give as much information as may be obtained by the single posterior anterior and lateral views Without question, the best secondary view to be obtained should be the lateral chest film either right or left, depending upon the side in which the tumor lies The lateral chest film not only completes the three-dimensional view of the tumor mass but definitely localizes its position in the front, middle or back of the chest which aids greatly in the differential diagnosis for different tumors have certain choice locations for their occurrence

Chest films, both posterior-anterior and lateral, made with increased penetration for bone detail may show bone erosion or destruction or the presence of calcium or bone or teeth within the tumor mass which is of distinct help in differential diagnosis *Planigrams* in the posterior-anterior or lateral position or both may give valuable information as to location, density, softening or cavitation, the presence or absence of calcium or bone, and some detail as to narrowing, displacement or compression of trachea or bronchi, and the width of the subcarinal angle *Posterior anterior and lateral chest films made with the esophagus filled with barium* may also aid in the localization and differential diagnosis as to whether tumors are of the mediastinum or closely related to it, such as intramural esophageal tumors, diverticulae, esophageal wall tumors, diaphragmatic hernia and other mediastinal masses Visualization of the stomach, small intestine and colon may help considerably in eventration or displacement of the diaphragm, in diaphragmatic hernias, and at times in reduplication of intestinal segments

A *roentgenokymogram* may occasionally be of value in helping to determine whether a given mass presents an expansile or transmitted pulsation in a differential diagnosis between an aneurysm and a tumor riding on the aorta or pericardium *Bronchograms using iodized oil or dionosil or one of the other opaque media* may reveal bronchial tumor, stricture or obstruction, tracheal or bronchial compression or displacement, and at times may reveal a cavity or abscess communicating with a bronchus They may also clearly show the displacement of the lung by tumor or pleural fluid accumulation, and at times may outline a fistula between bronchus and esophagus *Fluoroscopic study* may enable one to recognize pulsation, shifting, the angles of one organ with another, and last of all, diaphragmatic motion

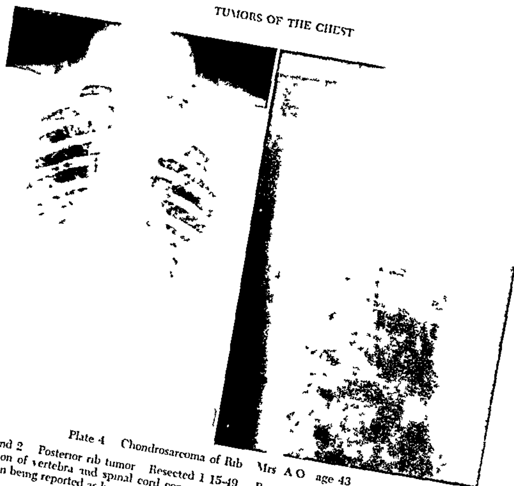


Plate 4 Chondrosarcoma of Rib Mrs A O age 43

Fig 1 and 2 Posterior rib tumor Resected 1 15-49 Reported as osteochondroma Recurred with invasion of vertebra and spinal cord compression September 1949 Laminectomy Tumor removed again being reported as benign osteochondroma

Diagnostic Pneumothorax or Pneumoperitoneum

Diagnostic pneumothorax or pneumoperitoneum may be used to advantage upon occasion to differentiate between tumors of the chest wall and the lung or between one in the mediastinum or in the lung or to separate the lung from the diaphragm to more clearly outline a mass in this region Aspiration of pleural fluid and its replacement with air may clearly visualize pleural deposits or underlying tumor in the lung chest wall or mediastinum which has been obscured by the fluid Diagnostic pneumoperitoneum may help to differentiate between masses in the liver or in the diaphragm and those lying in the mediastinum pericardium or lung

DIAGNOSTIC PROCEDURES

THORACOSCOPY

Thoracoscopy may at times give information to establish the diagnosis and perhaps save the patient an unnecessary thoracotomy When used after diagnostic pneumothorax or after fluid has been aspirated from the pleural space and replaced with air one may through the thoracoscope recognize tumor implants on the surface of the lung or pleura and through a secondary opening may obtain biopsy material to establish the diagnosis of a malignant process that has metastasized to the pleura this may save the patient an unnecessary

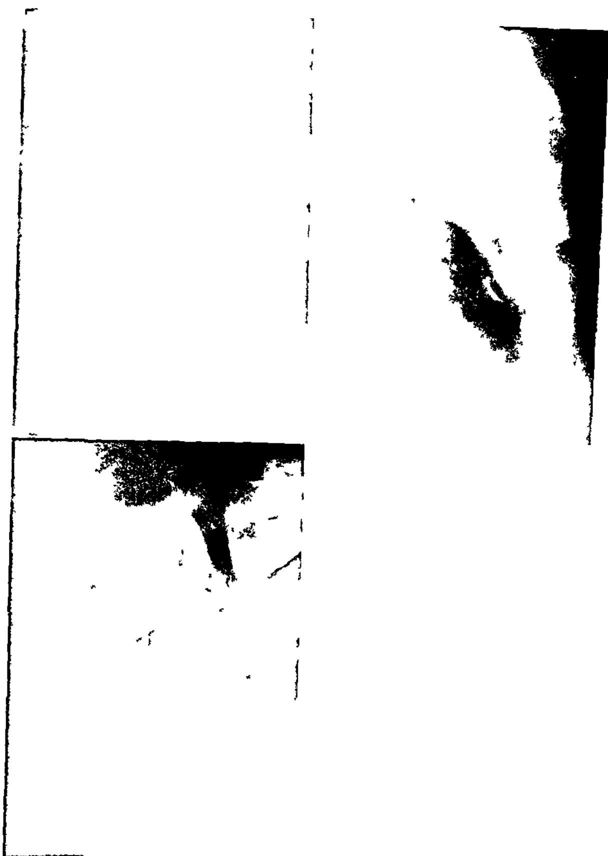
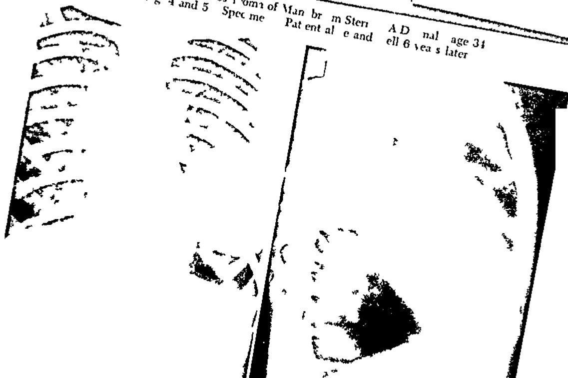
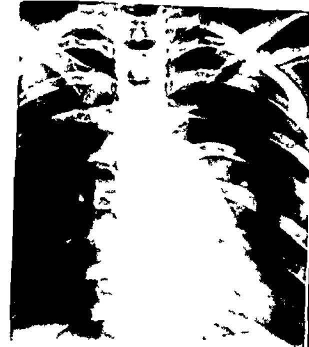


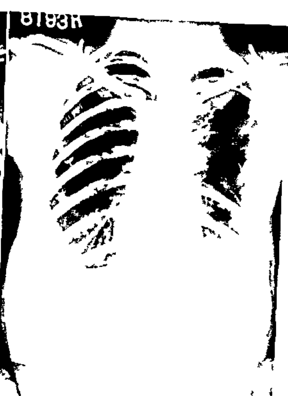
Plate 5 Chondrosarcoma of Manubrium Sterni A D male age 34

Fig 1 and 2 Posterior anterior and lateral x ray Tumor mass growing Patient had been operated upon 2 years before Biopsy reported as benign Tumor curetted and bone chip graft inserted
Fig 3 Detail x ray of tumor New bone islands from bone graft

Plate 5 Chondrosarcoma of Manubrium Sterni A D nal age 34
Fig 4 and 5 Specimen Patient alive and well 6 years later







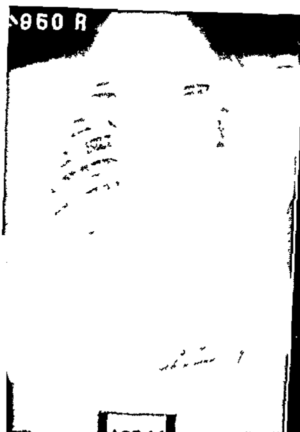




Plate 7 Malignant Giant Cell Tumor of Rib E S female age 32

Fig 1 Local soft tumor with rib destruction posterior sixth rib (in circle) Spontaneous intra pleural hemorrhage later

Fig 2 Following incomplete removal of tumor Vertebral body involved

Fig 3 Recurrence of tumor Poor response to x ray treatment Patient died 4 years after original surgery



Plate 8 Lipoma Dumbbell Axillary M S male age 54

Fig 1 and 2 Lipoma extra pleural in right chest wall and in axilla Note slight density of tumor

thoracotomy and prove the condition is not amenable to surgery with any hope of cure

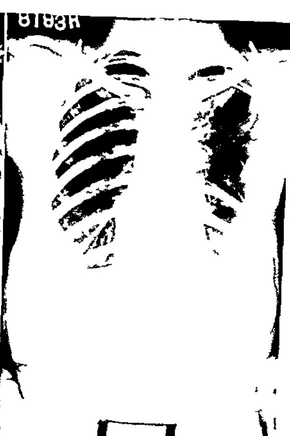
NEEDLE BIOPSY

Direct needle biopsy of peripherally located chest tumors may furnish biopsy material to permit a definite diagnosis of the nature of the presenting tumor It should not be used as a routine measure in a patient otherwise suitable for surgery but probably should be confined to the patient unsuitable for major surgery for one of many reasons and in whom a pathological diagnosis is desirable before resorting to radiation therapy intravenous injections or similar nonsurgical treatments It is of little value in the more centrally developing malignant processes The procedure itself is not wholly without risk as serious bleeding can be initiated and dissemination of infection as well as tumor cells can be brought about in this way

LABORATORY STUDY

It goes without saying that *all* patients presenting chest tumors should have a routine examination of urine and blood including at least a hemoglobin leukocyte and differential count and sedimentation rate A low hemoglobin reading may be an indication of serious bleeding which has occurred or of the cachexia resulting from a malignant tumor Alterations in the leukocyte count may give a clue to an inflammatory process to necrosis of a tumor mass or to leukemic process otherwise unsuspected In like manner the differential count may suggest a leukemic process pyogenic infection or an eosinophilic disturbance The sedimentation rate may be elevated in





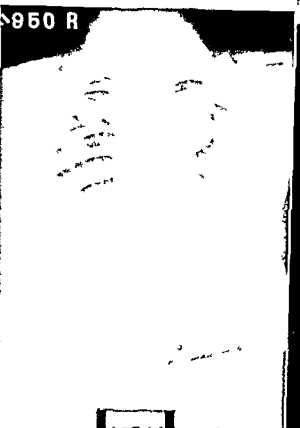




Plate 7 Malignant Giant Cell Tumor of Rib E S female age 37

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infection abscess carcinoma necrosis of tissue and pleural effusion

The urine examination for sugar is important because of the special care needed in surgery upon the diabetic The finding of albumin or sugar or abnormal cells gives the clue to a malignancy of the bladder or a hypernephroma or renal tuberculosis which may be significant in the consideration of the presenting lung mass Such findings may give the clue to indicate intravenous *urography or cystoscopy* and retrograde pyelograms or ureteral cultures for better evaluation of the urinary tract Renal function studies may be indicated and in some cases liver function studies should be made in patients with a history of jaundice liver enlargement or suspected liver *metastasis*

BONE MARROW BIOPSY

Sternal bone marrow biopsy may be particularly valuable in patients with lymph node enlargements in whom it may occasionally give information concerning a blood dyscrasia or may show the granulomas of sarcoid or tuberculosis and rarely metastatic tumor

SPUTUM STUDY

Careful examination of the sputum may suggest bronchiectasis *lung abscess* or empyema with bronchial fistula depending upon *whether it is pure pus mucopurulent or foul* smelling The presence or absence of blood should also be noted The presence of hair or greasy material suggests a draining dermoid Bits of tissue should be examined microscopically for carcinoma *or other tumor* Microscopic study of the sputum fresh or preserved for tumor cells in the hands of experienced pathologists is a valuable method for diagnosing carcinoma of the lung but unless a rather wide experience has been acquired it can lead to serious error An in*flammatory lesion such as bronchiectasis* can produce cells easily confused with malignant cells

Sputum smears should be routinely examined for the presence of tubercle bacilli Tuberculosis is frequently hidden and obscured by or confused with other conditions Special cultures for tubercle bacilli should be almost routinely made on patients who have cough or expectoration *Exploration or definitive* surgery for carcinoma should not be delayed however for the 6 or 8 weeks necessary for reports on such cultures if malignancy is strongly suspected Culture for secondary organisms and sensitivity studies should frequently be made in order that the proper *antibiotics for control of the predominant organisms* may be accurately determined Fresh potassium hydroxide preparations of sputum may reveal fungi of clinical significance Cultures for fungi on special culture media may be diagnostic under certain conditions but care must be used in interpreting the findings *because of the number of saphrophytes present*

Pleural fluid if available must be studied bacteriologically by smear and culture for secondary organisms and for tubercle bacilli Negative culture for tubercle bacilli does not necessarily rule out tuberculosis for even in *the presence of known clinical tuberculosis* over half of these fluids will not show organisms on either smear culture or guinea pig innoculation A bloody pleural fluid on first tap is strongly suggestive of malignancy primary of metastatic though it is occasionally seen in the presence of benign tumors tuberculosis *and other inflammatory lesions* The presence of blood in fluid obtained at *subsequent aspirations is* less significant as it is frequently traumatic in origin A search for malignant cells in pleural fluid should always be made and may confirm the diagnosis of a malignant lesion A bloody pleural *effusion containing malignant* cells is more often the result of a primary bronchogenic carcinoma than metastatic tumors but there are exceptions to this finding Diagnostic errors may easily be made on certain acute inflammatory lesions which produce cells showing mitotic figures closely resembling malignant cells

BRONCHOSCOPY

Bronchoscopic examination carefully done by an experienced bronchoscopist thoroughly

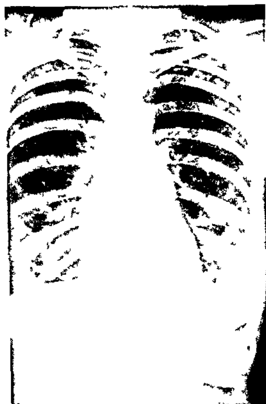


Plate 9 Neurofibroma of Chest Wall M S female age 20

Fig 1 Tumor left base laterally Palpable mass left lateral chest wall Extrapleural neurofibroma of intercostal nerve



Plate 10 Neurofibroma of Brachial Plexus Mrs F W age 24

Fig 1 Tumor removed through cervical incision preserving trunks of plexus Only slight area of anesthesia in ulnar area persisted

familiar with normal intrabronchial relationships and their variations is of extreme value in diagnosis and at times in treatment of intrathoracic diseases This inspection must not only include visualization of the larynx and vocal cords tracheal walls and the major bronchi for intrinsic lesions but must record evidences of displacements abnormal pulsations external rigidity or compression alterations of the subcarinal angle and positions of various secondary orifices resulting from extrinsic causes Localization of the source of secretions or bleeding may be equally as valuable as the visualization of a tumor Recognition and removal of a foreign body of extrinsic or of local origin may be of help Inspection of the larynx and vocal cords should also be made Paralysis of the left vocal cord from malignant infiltration under the aortic arch is a not infrequent complication of carcinoma of the lung

Since the introduction of telescopes which may be introduced through a bronchoscope the field of bronchoscopic visualization of the major bronchi secondary and even at times a portion of the tertiary divisions in some segments has been greatly enhanced Right angle telescopes permit the visualization of the orifices of the upper segments of right and left upper lobes which cannot be seen through the direct bronchoscope The fore oblique telescopes in like manner facilitate the exploration of the middle lobe and the lingula and some of the basal segments The retrograde telescope has a very restricted field of usefulness The use of curved aspirating tubes

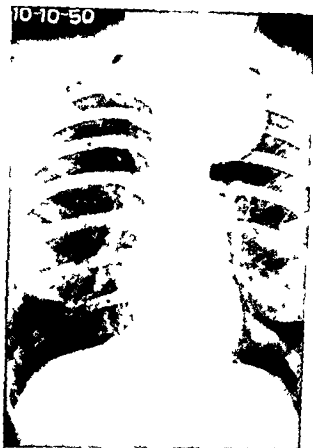


Plate 11 Neurofibroma L female age 26

Fig 1 Neurogenic tumor Fig 2 Pressure erosion of rib by benign tumor

and curved forceps may occasionally obtain material not otherwise obtainable

ESOPHAGOSCOPY

Esophagoscopy can be equally helpful not only in diseases of the esophagus but in some processes originating in adjacent structures Recording of displacements compressions bulgings pulsations perforations and so forth may aid greatly in making the final diagnosis of certain intrathoracic conditions Compression of the esophagus by a vascular ring or its perforation by a bronchogenic carcinoma are only two examples of the help that may be obtained in this way

BRONCHIAL AND ESOPHAGEAL BIOPSY

Biopsy of intrinsic masses in the bronchial or esophageal lumen offer one of the best means of arriving at a positive diagnosis At times biopsy through the normal mucosa in the region of the carina will give evidence of submucosal carcinomatous infiltration extending well beyond the limits of visible tumor

BRONCHIAL WASHINGS AND ASPIRATED MATERIAL

In the absence of definite biopsy material microscopic and cultural studies of material aspirated from the bronchial tree or obtained by irrigation and aspiration from a certain isolated segment may demonstrate carcinoma cells or the causative organism of an inflammatory process These should be almost routine when tissue cannot be obtained in any other way

LYMPH NODE BIOPSY

Biopsy of presenting lymph nodes particularly from the axillary or cervical region, may



Plate 12 Neurofibroma E B K male age 52

Fig 1 and 2 Posterior neurogenic tumor
Fig 3 Specimen Dumb bell tumor removed through posterior thoracotomy and laminectomy incisions simultaneously *Intraspinal extradural protrusion indicated by arrow*



Plate 13 Ganglioneuroma C J J female age 7

Fig 1 and 2 Large tumor in small child Trachea displaced Patient had temporary Horner's eye syndrome following surgical removal of tumor

furnish material to establish a diagnosis of carcinoma sarcoid tuberculosis or lymphoblastoma Information may at times be obtained by resection of the fat pad overlying the scalenus anterior muscle on one or both sides with microscopic section of the small lymph nodes contained therein This material is especially valuable in carcinoma of the lung lymphoblastoma and sarcoid particularly the latter

It must not be assumed that this entire battery of examinations and tests must be carried out on every patient who presents a thoracic tumor or a suspicion thereof in fact not even a small fraction of them may be necessary or advisable for the majority of tumors encountered In certain situations many of them may be necessary or advisable whereas in other situations the whole battery of tests may not add anything in a diagnostic way to the information that can be obtained by simple posterior anterior and lateral chest films One can literally spend hundreds of dollars of the patient's money and much of his time and energy to no avail Good clinical judgment here may mean a great deal to the patient's pocket book The exact nature of many thoracic tumors cannot be accurately diagnosed preoperatively even if every test in the book is applied prior to surgical intervention

It makes no difference to the patient in many instances whether an exact diagnosis is made beforehand or not If the tumor is there and the relative chances of its being benign or malignant are known and if it must be removed there is really nothing to be gained by any additional examinations Frequently the surgeon with the lesion before him cannot tell exactly what it is and the pathologist may be able to reach an accurate diagnosis only after extensive study The



Plate 14 Calcified Fibrous Tumor L J female age $12^{1}/_{2}$

Fig 1 and 2 Tumor explored at age of three and one half but not removed because of dense attachments terrific bleeding and biopsy report of sarcoma Nine years later tumor removed using 22 pints of blood Benign fibrous tissue tumor—neurogenic or mesothelioma with marked calcification Recovery

diagnostic studies therefore should be held to the minimum consistent with careful work in determining what therapeutic procedure should be followed By and large there are not many chest tumors which may be trusted very far There are too many malignant tumors among them and even a number of the benign tumors may cause serious trouble for the patient Taken as a whole the majority of them are best treated by surgical means There is only one location in the chest namely the anterior pericardiophrenic angle in which the majority of the conditions encountered may be treated by observation only with little chance of serious complications In all others the percentage chances of trouble are too great to be ignored

SURGICAL APPROACH

Direct surgical approach to the tumor itself is indicated in most chest wall tumors except the intrathoracic neurogenic tumors for the majority must be excised en masse because of their malignant potentialities It is well to remember in approaching such tumors that the reconstruction of the chest wall must be accomplished consequently due thought must be given to the placing of the incision and to the saving of the flat muscles pectoralis major seratus anterior and latissimus dorsi for subsequent use in the reconstruction procedure



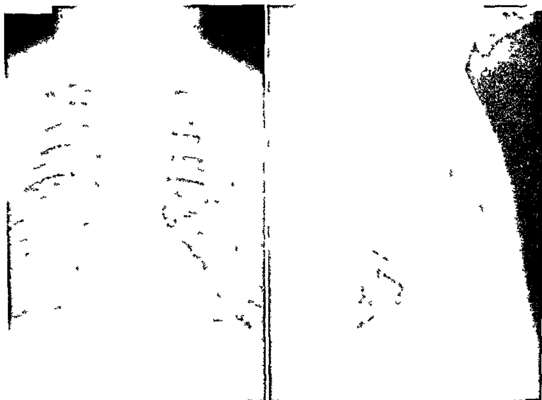


Plate 16 Neurofibroma of Vagus Nerve (Von Recklinghausen s Disease) or (Multiple Neurofibromatosis) P E male age 20

Fig 1 and 2 Patient an epileptic for several years with frequent seizures in spite of medications Has had no attacks in nearly a year following removal of tumor Left vagus nerve trunk excised proximal to origin of recurrent nerve

The maximum amount of bony chest wall consistent with the proper surgical treatment of the lesion must be conserved for stabilization purposes in conjunction with muscular or fascial transplants wire mesh or plastic prostheses

The anterior intercostal approach with section of one or two cartilages is adequate for the removal of small anterior mediastinal tumors such as cysts thymomas smaller teratomas pericardiophrenic angle cysts and if structures are not too adherent middle lobe lobectomy Lobectomy or total pneumonectomy may be carried out through this exposure but some of the other exposures are more convenient For some of the larger anterior mediastinal teratomata total thymectomy and for some cardiac work a bilateral curved submammary incision with bilateral intercostal incisions and transection of the sternum at the level of the third or fourth interspace opening both pleural cavities affords excellent exposure A low cervical collar incision with vertical extension down the midline into the thorax with splitting of the sternum may give adequate exposure for deliverance of the large substernal mass through the superior aperture in the thorax It is well to remember however that many of these tumors when freed from their upper attachments and their blood supply may be delivered through the collar incision without the necessity of splitting the sternum if intratracheal anesthesia is used to maintain a free airway

The direct lateral approach with or without the resection of one rib with the patient lying on the contralateral side affords excellent exposure for the majority of intrathoracic



Plate 17 Neurofibrosarcoma A deC male age 2
Fig 1 and 2 Patient died from pressure from tumor

ons for the lung anterior and posterior diastinum are readily accessible It has disadvantage in the patient who has pro pulmonary secretions which tend to flood dependent lung and interfere with aera and in the case of tuberculosis where h aspiration may bring about bronchogenic ead of disease This is not as important with adequate chemotherapy available t was previously when no such protection at hand It has the added disadvantage of eding the expansion of the dependent predisposing to carbon dioxide buildup changes in the hydrogen ion concentra of the blood unless the anesthesiologist pecially vigorous in his assisted respiration he posterolateral approach with or with resection of a rib likewise gives adequate osure for most intrathoracic work The ent may be either completely prone or d slightly to the opposite side Respira tory activity of the opposite lung is freer and the risk of aspiration is reduced in this posi tion If at the same time the patient is sup ported by pads or balloons under the thorax and under the hips avoiding any pressure on the abdomen or if the patient is suspended on one of the special tables designed for that pur pose respiratory excursions are impeded less than in almost any other position except the dorsal recumbent The completely prone position is especially valuable for approach to posterior neurogenic tumors which may have an intraspinal extension for in this position a hemilaminectomy may be carried out simul taneous with the thoracotomy for complete re moval of the tumor in one stage The level at which the incision is made and its shape must be determined by the position of the tumor to be removed and its probable attach ments

Certain tumors particularly of the mid or



Plate 18 Sympathicoblastoma S S female *age 6 months*

Fig 1 Mal gnant tumor of sympathetic trunk with Horner s eye syndrome Pat ent d e l 2 montl s l ter with metastases



Plate 19 Sympath coblastoma J B female age 4 months

Fig 1 an l 2 Large tumor left upper chest poster orl Pat ent d ed th metastases

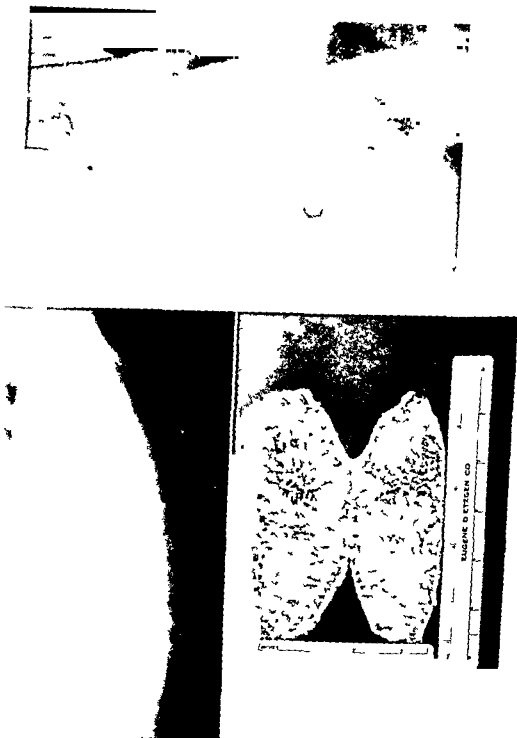


Plate 20 Benign Giant Cell Tumor of Sternum A K male age 33

Fig 1 Photo of chest wall tumor
Fig 2 Lateral x ray of sternum

Specimen Tumor developed following injury to sternum Body of sternum resected and reconstructed with bone and fascial graft



Plate ?1 Ben g F b oma of D pl a m M K fe nale age 64

F g 1 and ? Tun or of te o h lf of d pl agm
F g 3 Photo of chest all Pro ect o of tumo bet een r bs
F g 4 Spec men Benign fibroma Exc sed and diaph agm reconstructed Reco ery



Plate 23 Diaphragmatic Hernia—Traumatic E B female age 65

Fig 1 and 2 Posterior anterior and lateral chest film
Fig 3 Large loop of colon in left pleural cavity Traumatic diaphragmatic hernia Auto accident 23 years before Transthoracic repair Recovery

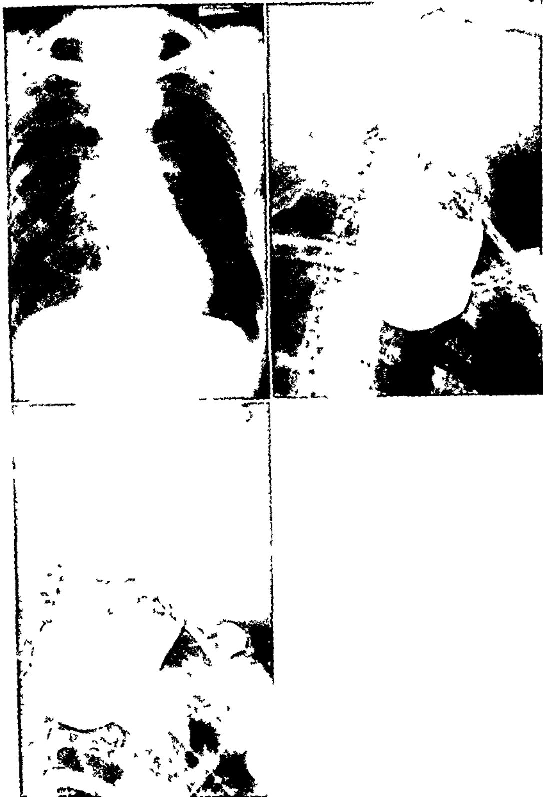


Plate 24 Pharyngeal (Zenker's) Diverticulum C F male age 67

Fig 1 Food filled diverticulum extends into upper mediastinum and resembles mediastinal tumor
Fig 2 Barium filled diverticulum One-stage resection Recovery



Plate 27 Dermoid Cyst of Anterior Mediastinum R S male age 24

Fig 1 Lateral chest x ray film This tumor did not show on posterior anterior film The patient expectorated hair and sebaceous material for 2 years but the tumor was not discovered because a lateral x ray film was not made

legs must be elevated at frequent intervals to drain out the veins and active motion encouraged Tensor bandages should be kept snugly applied in an attempt to avoid postoperative thrombosis Fowler s position with the knees flexed over a break in the bed should be avoided as should too much dangling with the legs hanging over the edge of the bed The legs must be checked frequently for cramps tenderness or swelling in the calves If these appear anticoagulant therapy should be instituted promptly The patient must be encouraged to move cough and raise and to get out of bed at the earliest possible moment consistent with his safety Drains and suction tubes should be removed as early as is consistent with maintaining expansion of the lung and removal of intrapleural secretions Sedatives should be used to keep the patient relatively comfortable but *not to knock him out* Fluid intake should be maintained so that an adequate urine output is produced Food and fluid should be taken *by mouth as early as possible for the patient s* own good and well being

The patient who understands from the start what the *postoperative care* will be *usually* cooperates well and is much happier than one to whom each manipulation comes as an extra burden The patient who is encouraged to be active and do things for himself recovers much more promptly than the one who is encouraged to become an invalid Patients who have had extensive resections or pneumonectomy must be watched more carefully

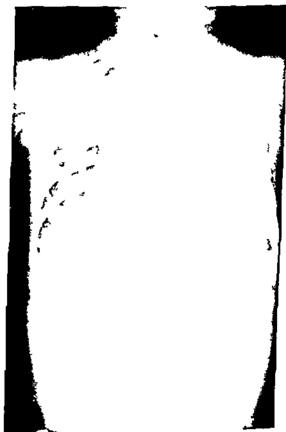


Plate 28 Benign Dermoid Cyst P R female age 11 months

Fig 1 Huge dermoid cyst of mediastinum *removed surgically* Discovered following pneumonia and aspirated on several occasions as pleural effusion

than some of the other patients because these things are more frequently done in elderly individuals with some cardiac impairment. Cardiac irregularities or fibrillation occur in roughly ten per cent of this group and may be induced by giving a little too much intravenous fluid or blood, by straining at stool or following an enema, or by unbalanced intrapleural pressures or shift of the mediastinum.

TUMORS OF THE CHEST WALL

GENERAL CONSIDERATION

Tumors of the chest wall exclusive of those arising in the breast or subcutaneous tissues are not commonly seen. They may present as a visible or palpable external mass, a few of them reaching huge proportions. Many originating in the thoracic wall or within it give no external evidence of their presence. Tumors of even a small size may erode or destroy a rib. Those arising in a small space may produce pain at an early stage and be discovered because of it. Many, however, including some of considerable size, are completely silent and are discovered only on routine x-ray film, in surveys, or during the course of a general examination including chest fluoroscopy, or on routine chest films.

For purposes of classification, they may be divided as follows:

BENIGN TUMORS

Chondroma
Osteoma
Osteochondroma
Hemangioendothelioma
Neurogenic Tumors: Neurofibroma (Fibroma, Neurilemmoma, Schwannoma); Ganglioneuroma; Pheochromocytoma (Paraganglioma)
Xanthoma
Lipoma
Hemangioma
Cystic Hygroma
Dermoid Cyst
Meningocele

PSEUDOTUMORS

Lung Hernia

MALIGNANT TUMORS

Sarcoma: Osteo-chondro-myxo-fibro-lipo-sarcoma
Ewing's Tumor
Sympathicoblastoma
Myeloma
Malignant Mesothelioma

METASTATIC TUMORS

Breast
Lung
Hypernephroma
Sarcoma
Carcinoma of the Thyroid

INFLAMMATORY LESIONS

Chondritis: Tuberculosis; Actinomycosis; Brucellosis; Typhoid Fever
Osteomyelitis
Empyema Necessitatis
Chest Wall Abscess
Encapsulated Empyema
Eosinophilic Granuloma

BENIGN TUMORS

Chondroma, Osteoma, Osteochondroma

These benign tumors arise from rib or cartilage, most often the former. They are found more commonly in the anterior thorax, though rarely a chondroma may develop posteriorly from the articular facets or the intervertebral discs. They may be small when discovered but many reach considerable size before they attract much attention. If palpable, they present as a rounded or ovoid mass of firm to hard consistency though occasionally there are cystic areas. They are fixed in position, without overlying skin or soft tissue attachments. About half of them are accompanied by pain which often precedes their discovery by several months. A preceding history of local trauma may be obtained in nearly half of the patients, though trauma is not necessary for their development. Some of them reach huge size before they are discovered or at least before the patient seeks relief.

They may be made up entirely of cartilage (chondroma), entirely of bone (osteoma), but more commonly are a combination of the two (osteochondroma), with or without myxomatous change. Chondromas do not usually

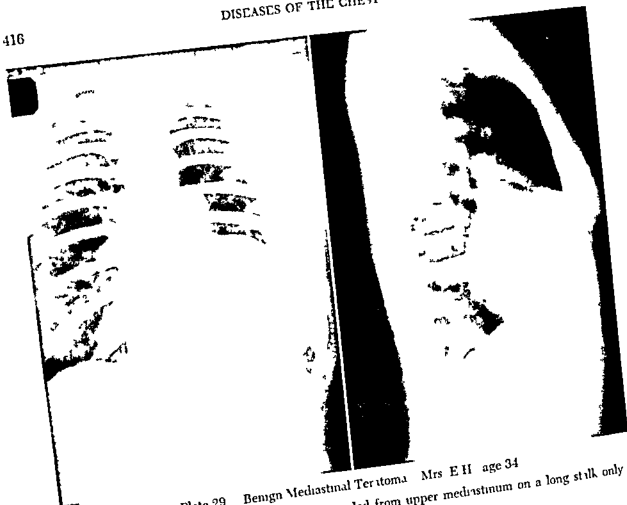


Plate 29 Benign Mediastinal Teratoma Mrs E H age 34

Fig 1 and 2 Anterior mediastinal tumor extruded from upper mediastinum on a long stalk only 1 cm in diameter

arise from the costal cartilage but more commonly near the anterior end of the rib or develop in the anterior end of the rib as an enchondroma The growth of this type of tumor is usually very slow and may extend over a period of many years the tumor reaching huge size by this time When small the tumors may involve but one rib but after years of continued growth they may extend and involve adjacent ribs or other structures

Chondromas appear as a localized smooth or nodular mass on the roentgenogram but may suggest cystic change The osteomas present as an irregularly expanding bony lesion of a sclerotic type Osteochondromas may present a picture similar to chondromas but are more likely to show irregular mottled areas of calcification within the tumor mass Microscopically the tumors present a picture of mature cartilage or bone or both although frequently it is not entirely normal in appearance Cross sections of the tumor may not be of uniform appearance, hence errors in diagnosis may easily be made from small biopsy specimens alone This is especially true when such tumors have undergone malignant change which may be evident only in certain areas of the periphery of the tumor The frequency of recurrence of these tumors following very restricted local excision suggest that at least some of them which microscopically appear to be benign are really low grade sarcomas Local sclerosis of bone costochondral separation healed in malposition or exuberant callus from an unrecognized rib fracture are mistaken not infrequently for a bone tumor

Treatment The fact that these tumors are not radiosensitive the uncertainty of an accurate diagnosis from a biopsy specimen and

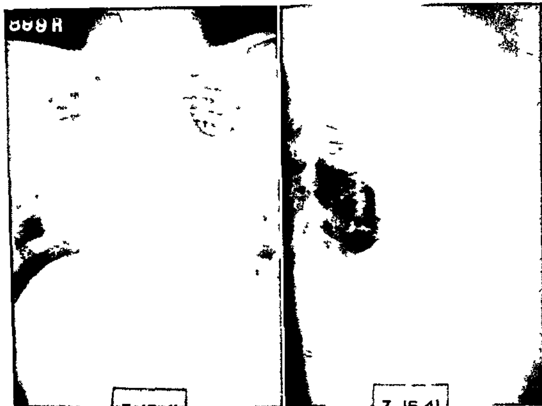


Plate 30 Benign Teratoma G M male age 22

Fig 1 and 2 Huge anterior mediastinal tumor Patient died from mediastinal obstruction 2 hours after admission to hospital

the frequency of recurrence following very local excision makes surgical resection of a rather radical type the procedure of choice These tumors must not be shelled out but should be resected en masse with a wide margin of normal rib cartilage intercostal muscle and pleura if recurrences are to be avoided Reconstruction of the chest wall and its stabilization by a plastic procedure using fascia muscle bone graft wire or plastic mesh should be done as a part of the primary operation While the results from resection of benign tumors are good those for malignant lesions are much less favorable

Hemangioendothelioma of the Rib

This rare benign tumor of the rib apparently develops from within destroying the cortex of the rib as the tumor mass expands perhaps with pathological fracture and local tumor mass frequently suggesting a malignant tumor Local excision is curative Similar lesions may occur elsewhere at a later date and should not be interpreted as metastases as the lesion is reported to be multicentric in origin

Neurogenic Tumors

Neurogenic tumors such as neurofibromas ganglioneuromas are ordinarily classified with the posterior mediastinal tumors but are truly of chest wall origin arising either from an intercostal nerve ganglion or sympathetic nerve trunk This group are variously called fibromas neurofibromas lemmomas neurilemmomas Schwannomas and perhaps also some altered ones classified as xanthomas theoretically arising from the nerve sheath of Schwann They are fibrous tissue tumors and contain no nerve elements Ganglioneuromas arise from the sympathetic root ganglia and contain

ganglion cells and nerve fibrils The *majority* of these tumors arise posteriorly and remain within the thoracic cage though occasionally one may send a palpable projection out between the ribs More rarely one may develop from an intercostal nerve anteriorly and peripherally in the chest wall All of them arise extrapleurally They may develop from any medullated nerve in any part of the body but are apparently more frequent in the chest usually in the above described position though rarely one is seen in the phrenic or vagus *nerves*

The patient presenting them usually has no indications of Von Recklinghausen s disease (multiple neurofibromatosis) and shows neither the cafe au lait spots nor the multiple cutaneous and subcutaneous nodules of this condition The patient with Von Recklinghausen s disease may present hundreds of these tumors throughout the body with literally dozens of them of small size along each intercostal nerve giving the nerve a rosary bead appearance which is usually not seen on the x ray film Occasionally however they may be demonstrated by x ray in this condition When any of them become large or grow the possibility of malignant change must always be considered

Neurogenic tumors commonly present in the *posterior aspect* of the chest as a smooth rounded or ovoid shadow of fair density lying in the costovertebral gutter hugging the vertebral body In size they vary from very small (2 cm in diameter) to huge tumors which may fill the entire *hemithorax* They are usually not calcified though occasionally when degeneration of the *tumor has occurred* they *may show* irregular calcium deposits When a portion of the tumor has inserted itself between the ribs there may be *thinning* and a smooth extrinsic pressure *erosion of the rib* with widening of the interspace The periostium of the rib however is smooth and intact in contrast to the rib erosion *seen with* malignant tumor

A small percentage of these tumors perhaps ten per cent show a collar button or dumbbell like extension along the intercostal nerve through the intervertebral foramen to present as an *intraspinal* extradural tumor mass with or without secondary cord symptoms from *pressure* A *smooth erosion* or widening of the lateral foramen of the vertebral pedicles may be *demonstrated* on x ray examination again *in contrast to the* irregular erosion of malignant disease These tumors may arise at any level *in the thorax* through probably they are more frequent in the upper half

The majority of these tumors *produce* few or no symptoms Pressure erosion of rib or the vertebral pedicles may give *lateral chest* pain or aching The tumors which arise in the sympathetic trunk in the upper posterior chest above the third dorsal level may in their growth produce interruption of the trunk and a typical Horner s eye syndrome (ptosis myosis enophthalmos and anhydrosis) Such findings may likewise occur following the surgical removal of a tumor so located even though the tumor itself had not produced it beforehand Rarely does such a tumor produce pleuritis the pleural cavity usually being free of adhesions though occasionally a pleural effusion develops Increased growth may produce pressure symptoms Such growth usually occurs very slowly over a long period of time Rapid growth with the production of an effusion should raise the question of malignant change though it does not necessarily indicate it The majority of these tumors are benign but there is a very definite incidence of malignant (sarcomatous) change estimated as about 37%

Treatment There is usually *little question* as to the location of these tumors Should one be concerned about the possible origin of the shadow of these in the chest a diagnostic pneumothorax will usually show *the lung to* be free pulling away from the tumor and not infrequently showing a crescentric *defect in* its substance from prolonged pressure of the tumor on the local pulmonary parenchyma Even though the tumor is discovered accidentally *and is asymptomatic*, it should be *removed* surgically The tumors are not radiosensitive and tend to grow and cause local *symptoms* and may undergo malignant degeneration The risk of removal of a large tumor may be somewhat greater than that of a small one

The surgical approach is ordinarily directly

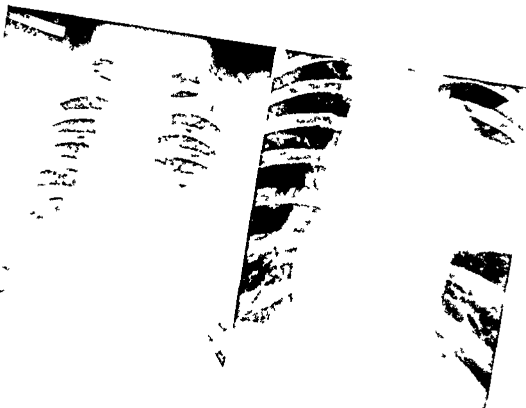




Plate 31 Malignant Mediastinal Teratoma G L male age 22

Fig 1 November 1937 Tumor

Fig 2 January 1940 Tumor

Fig 3 Specimen Patient died of pulmonary embolism 12 days after operation



Plate 32 Bronchial Cyst M E H female age 9

Fig 1 and 2 Large anterior mediastinal mass Bronchial cyst of anterior mediastinum

over the tumor for best exposure The pleura over the mass may be incised and usually can be wiped back and the tumor dissected out of its bed without too much difficulty The blood supply from the intercostal vessels may be quite rich and must be adequately controlled Bleeding from the bed may be quite brisk if the intercostal vessels are torn The incoming nerve or nerve trunks particularly the intercostals should be picked up and ligated for occasionally a projection of dura along an intercostal nerve reaches out far enough so that it may be opened and spinal fluid leakage result unless care is exercised Care must be taken not to evulse the nerve roots and the vessels accompanying them through the intervertebral foramen or damage may be done to the cord or intraspinal bleeding be initiated

If it is evident that the tumor extends through the intervertebral foramen a laminectomy should be performed at once and the nerve roots ligated and sectioned so that the intraspinal extradural portion of the tumor may be removed The prone position of the patient on the operating table is of distinct advantage in this situation If the tumor arises from the upper sympathetic trunk it is usually not possible to save the trunk when removing the tumor and a Horner s eye syndrome may be expected and accepted Should the tumor prove to be densely adherent at the time it is removed one should suspect malignant change although this does not necessarily follow Results from excision of these tumors is excellent if the tumor itself is benign

Pheochromocytoma (Paraganglioma)

More recently a few cases of the adrenalin producing tumor pheochromocytoma arising from the sympathetic trunk have been reported lying in the posterior thorax along the bodies

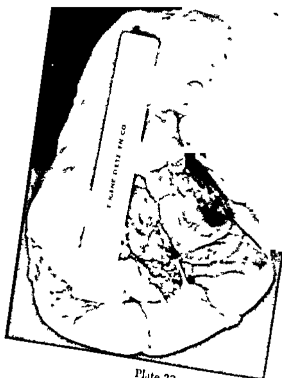


Plate 33 Benign Thymoma J T male age 12

Fig 1 and 2 Large anterior tumor

Fig 3 Specimen Removed through posterior approach



Plate 34 Benign Thymic Cyst L W, male, age 43
Fig 1 and 2 Mass of slight density lying far anteriorly Excised

of the vertebrae and presenting a shadow similar to that produced by a neurofibroma or ganglioneuroma The patient presenting the tumor in this situation may present hypertension, easy fatigue, nervousness, palpatation, dizziness, unusual sweating, to alert the surgeon to the possibilities of an adrenalin producing tumor Sudden sharp elevation of the blood pressure as the tumor is being manipulated may also warn him of such a condition, and proper precautions taken to reduce the blood pressure during the procedure and to sustain it following removal of the tumor If it is suspected preoperatively, special tests should be done before surgery is undertaken and the whole program planned to take care of the emergency situation when it arises

Xanthoma

This has been discussed under 'Neurogenic Tumors"

Meningocele

Rarely one may encounter in the posterior chest a spherical or dewdrop shaped mass of medium density running along the spine in the costovertebral gutter which is an intrathoracic extrapleural meningocele They are usually not diagnosed preoperatively, often because the possibility of such a condition is not considered It probably could be diagnosed by a reduction in its size following spinal drainage, by a myelogram or by needle aspiration They are usually asymptomatic and cause little or no trouble The surgeon should always be alert to the possibility of such a condition when confronted with a cystic tumor in this location Surgical excision must provide for control of spinal fluid leakage

Angioma, Hemangioma, Cystic Hygroma

Angioma of the chest wall, hemangioma or lymphangioma, or a combination of both, may



Plate 35 Lipoma of Mediastinum A S male age 50

Fig 1 Benign lipoma of anterior mediastinum removed surgically

be small and localized or may be huge and involve wide areas of the chest wall Quite a few are superficial and involve soft tissues only while a few extend deeper and may involve the ribs and deeper chest wall structures They usually present as soft spongy fleshy masses with or without pulsations Depending upon their makeup their color may be reddish blue or purple or the mass may show no color change being covered by normal skin They may have been present since birth and unchanged or may have shown rather constant increase in size If small and localized they may be easily cured by excision and even some of the larger masses may be successfully treated in this way Some of the larger masses especially those which involve rib or deeper structures may prove too extensive for excision and terrific bleeding may be encountered if the mass is entered in attempted excision Incomplete removal may be followed by local recurrence even though the process is not malignant The local use of pressure plus injection of sclerosing solutions may obliterate certain areas as may local irradiation or radium therapy

Lipoma

Lipomas of the skin and subcutaneous tissues occur very commonly Those involving the chest wall are not frequently encountered They vary in size from small to huge and not infrequently may have a dumb-bell character with some of the mass subcutaneous or subpectoral and the rest intrathoracic and extrapleural The total size of the mass may be very deceiving as much may be concealed in the axilla in the neck or in the mediastinum All in all they cause no trouble unless from their size they may produce pressure symptoms The external mass when palpated may present the characteristics of lipomata elsewhere with a lobulated semicystic feel If encapsulated or entrapped under a fascial plane this characteristic may be absent From the x ray standpoint lipomata may present less density as a given mass than some of the denser tumors If large or pro-

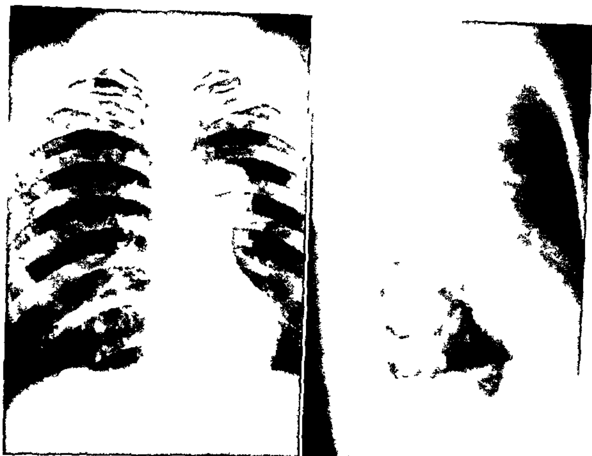


Plate 36 Bronchial Cyst of Mediastinum E DeG male age 31
Fig 1 and 2 Mass in mid mediastinum Benign bronchial cyst

ducing symptoms or if the diagnostic diagnosis is uncertain surgical removal is to be recommended They can usually be enucleated readily though they have a tendency to insert themselves around other structures with multiple finger like projections Rarely such a tumor will undergo malignant change as a lipomyxosarcoma

Benign Giant Cell Tumor

This tumor is extremely rare Most of the rib lesions occur posterior to the angle and most of the cases reported occurred in younger individuals The tumor presents as a local mass showing the characteristic x ray picture of giant cell tumor elsewhere Radiation therapy is adequate for the control of the condition if it can be diagnosed as a benign giant cell tumor with certainty If not local excision if it is in an accessible location is curative

PSEUDOTUMORS OF THE CHEST WALL

Rarely localized congenital or acquired defects of the chest wall may result in herniation of the lung through the abnormal opening the herniated lung presenting as a localized tumor mass The soft character the anterior location at the site of a previous injury or stab wound the increase or decrease with changes in respiratory pressures the resonant note to percussion and the area of increased radiability on x ray examination should easily establish the diagnosis Local repair of the chest wall defect with periosteal or fascial transplant after reduction of the hernia will bring about a cure

MALIGNANT TUMORS OF THE CHEST WALL

Primary malignant tumors of the chest wall although reported in slightly smaller numbers

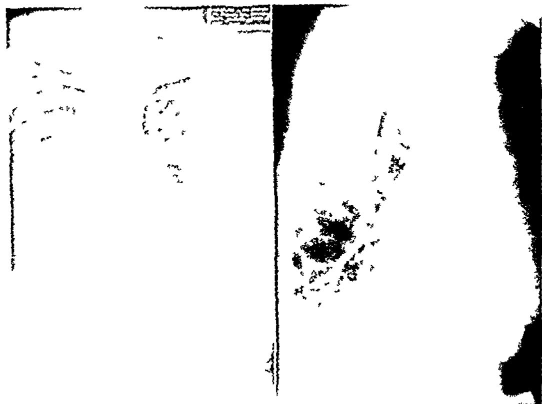


Plate 37 Celomic Cyst "Spring Water" Cyst of Mediastinum Mrs S age 54
Fig 1 and 2. Right anterior basal mass

than the benign tumors probably actually constitute 40 to 50% of tumors of the chest wall for a number of the tumors reported as benign have subsequently recurred and metastasized and probably were malignant from the start although unrecognized The possibility of malignancy must be considered in every chest tumor no matter how innocent it may appear to be

Sarcoma

Sarcoma may arise from cartilage or bone fat or fibrous tissue It may contain a single tissue only or many combinations such as osteo chondro lipo fibro sarcoma with or without myxomatous change The tumor usually presents as a mass with or without chest wall pain Not infrequently it has developed rather recently or a previously existing mass has recently increased in size The x ray picture may be characteristic with evidence of bone destruction but it may be identical with that of a benign tumor the diagnosis being made only after the tumor has been removed

Microscopically much of the tumor may present a benign picture with sarcomatous changes being evident only in peripheral portions of the tumor or in areas which have shown recent growth The incidence of recurrence of supposedly benign tumors of cartilagenous origin would make one suspect that a number of these were malignant from the start even though such a diagnosis could not be made at the time If it is in an accessible part radical excision including the adjacent pleura must be carried out if good results are to be obtained There is a considerable tendency for these tumors to recur as well as to give distant metastasis even under the most favorable circumstances

Ewing's Tumor

Ewing's tumor of the rib usually occurs in younger individuals (under the age of 20) It arises in the shaft of the bone rather than in the epiphysis and tends to involve the cortex and periostium of the bone rather than the medulla Pain may precede the appearance of the local mass by a few weeks or a few months There is *frequently a history of previous trauma* in the area Fever and leukocytosis often occur with it Tumors of this type usually do not show the onion skin formation which may be seen elsewhere The tumor has a considerable tendency to recur and to metastasize widely *Treatment* by wide excision followed by radiation has given a few 5 year results Treatment by radiation alone may *show* good response to the first radiation but poor on subsequent treatments

Malignant Tumors of Neurogenic Origin

Malignant tumors of neurogenic origin arising in the chest are usually seen in the posterior paravertebral region in the same areas occupied by the neurofibromas and ganglioneuromas Kent in 1944 reported that 41% of the tumors of neurogenic origin in this position were malignant and reported a 37% instance of malignancy from the cases reported in the literature Our own experience gives a malignancy rate well below the 41% reported Spindle cell or small cell sarcoma may be reported theoretically as a degeneration process of a neurofibroma Neuroblastoma and sympathicoblastoma are terms applied to the malignant tumors of ganglionic origin *Sympathicoblastomas apparently are seen more* commonly in the younger individuals and children Without evidence of metastasis or local bone erosion, it may be *impossible clinically* to even suspect malignant change in the tumor The microscopic picture establishes the diagnosis *Grossly in the operative field, the presence* of malignancy may be suspected if the tumor is unusually adherent or if evidence of direct bone invasion is encountered Sympathicoblastomas tend to metastasize early and rather widely The results from excision of *known malignant tumors* are not particularly good

There is often a serious question as whether the malignant process represents a malignant degeneration of a previously benign tumor or whether the tumor was malignant *from the* beginning Clinical evidence of growth in a tumor previously static or the development of *pain in a previously silent mass* would suggest that malignant change may have occurred in the tumor Because of this *distinct incidence* of malignancy in these *posteriorly* located tumors, it is the opinion of most thoracic surgeons that all of these tumors should be removed surgically without delay unless there is a serious contraindicating factor present

Malignant Giant Cell Tumor of the Rib

This is a very rare tumor Most of the reported cases occur in the rib posteriorly with destruction of the rib or adjacent vertebral body and transverse process, with the forma*tion of a local soft tissue mass which is usually* painful Complete radical removal would theoretically be the method of choice but this can rarely be accomplished Incomplete removal is followed by local recurrence Whether these represent sarcomatous change of the previously benign giant cell tumor or whether they were malignant from the beginning is uncertain Response to radiation is not particularly good

Myeloma

Occasionally myeloma may present itself as an apparently local tumor mass involving one rib or a local area of spine or sternum, where the process may remain apparently localized for a considerable period of time Its occurrence in a patient beyond 40 years of age, and the elongated sausage shape of the tumor mass should alert one to the possibilities of such a *condition* X ray studies of other ribs, skull and other bones for destructive areas should be made Disturbance of the albumin globulin *ratio may be suggestive* and a characteristic electrophoretic pattern in the blood *serum* may be seen early in the course of the disease Studies for *Benz-Jones proteins* in the urine may be disappointing since they are not constant even in evident myeloma A needle biopsy of the *tumor mass* may *definitely* prove the diagnosis Surgical resection rarely offers



Plate 38 Celomic Cyst "Spring Water" Cyst of Mediastinum Mrs S age 44

Fig 1 and 2 Huge anterior mediastinal cyst Large cyst of medium density—producing distention of veins of neck by pressure on superior vena cava

much of lasting value in these patients although occasionally the process may not become generalized for 2 or 3 years Radiation may be of value in relieving pain but the late results from the use of radioactive material are uncertain

Malignant Mesothelioma

This usually presents itself as a rather diffuse flat tumor formation usually on the parietal side not infrequently accompanied by a bloody pleural effusion Very rarely it may present as a localized tumor mass and be mistaken for one of the other intrathoracic tumors It may be easily confused with the pleural metastases of primary bronchogenic carcinoma hypernephroma and other malignant tumors

local pleural biopsy may be necessary to confirm it Surgical resection has nothing to offer and the response to radiation is not very encouraging

METASTATIC TUMORS

Metastatic involvement of the chest wall by malignancy originating elsewhere occurs more commonly than either the benign or malignant chest wall tumors It may occur from any malignancy but probably the most frequent are from carcinoma of the breast and carcinoma of the lung Recurrences in the chest wall following radical breast amputation for carcinoma will cause little difficulty in diagnosis If sharply localized occasional good lasting results may be obtained by radiation followed by a window type of excision and by reconstruction of the chest wall It is

only occasionally however that such results can be obtained

Direct invasion of the chest wall by a peripherally developing bronchogenic carcinoma occurs not infrequently. Occasionally when the peripheral tumor itself is small a local mass with chest wall pain will draw attention to the *condition which may be mistaken for a primary rib tumor*. Local excision of the chest wall with pulmonary resection may for a time give a good result but usually not a lasting one. Carcinoma of the thyroid and carcinoma of the kidney (hypernephroma) have likewise been reported as giving chest wall metastasis *to rib or sternum*. Metastases of this type may be pulsating, a characteristic not seen in other metastatic tumors. Their local removal may be accomplished but the results are not good over long periods of time. Sarcoma of soft tissue origin may at times give what is apparently a solitary metastasis to the chest wall or the periphery of the lung. Radiation therapy has more to offer for the majority of these metastatic tumors than does surgical excision. The effects are rarely long lasting.

INFLAMMATORY CONDITIONS SIMULATING TUMOR

There are a number of inflammatory conditions of the chest wall which for a time may simulate a chest wall tumor. Chondritis of the anterior costal cartilages with abscess formation may present a localized rounded tense swelling easily mistaken for a tumor of the cartilage. It may be caused by tuberculosis, typhoid fever, brucellosis or actinomycosis. They may be multiple in the parasternal region. A localized cold abscess in this region from suppuration of a lymph node lying along the internal mammary vessels may produce a similar picture. The diagnosis may not be established unless an exploring needle is inserted and pus encountered. The localized chest wall mass of a beginning empyema *necessitatis* from tuberculosis or staphylococcus may for a period of time be considered as a chest tumor. The encapsulated empyema from which it arises may have a rounded contour quite suggestive of a *tumor mass. The* history may give a clue, while the exploring needle may easily establish the true diagnosis. Conversely a malignant tumor may occasionally involve the skin and present a tender reddened mass closely *simulating a pointing* chest wall abscess.

The induration of an *actinomycotic cellulitis* of the chest wall *may for a time be confused* with a local *tumor. There is frequently* an associated process in the lung. The tendency to reach the skin and give abscess and sinus formation may help to establish the diagnosis. A localized osteomyelitis of the rib with associated abscess may for a time simulate tumor but usually it manifests itself quite soon as an inflammatory process. A localized area of sclerosing ostitis and periostitis may be confused with an early rib tumor. A localized eosinophilic granuloma of bone may likewise be easily mistaken for an early tumor.

THERAPEUTIC PROCEDURE SIMULATING TUMOR

The rounded dense homogeneous shadow of a localized therapeutic oleothorax may at times be confusing to one not familiar with this condition. The history and the tell tale needle puncture marks are of course a give away on the condition. Occasionally confusion may arise in the patient who has had an extrapleural pneumonolysis with an oil or paraffin extrapleural plombage. The irregular rib regeneration posteriorly at the site through which the operation was carried out may be mistaken for *rib destruction* by a tumor. If an intercostal approach or very limited axillary rib resection was used the picture may be all the more confusing. The history and of course *the* operative scars are diagnostic.

TUMORS OF THE STERUM

Tumors of the sternum are rarely seen. They may as in other tumors be primary benign, primary malignant, metastatic or inflammatory.

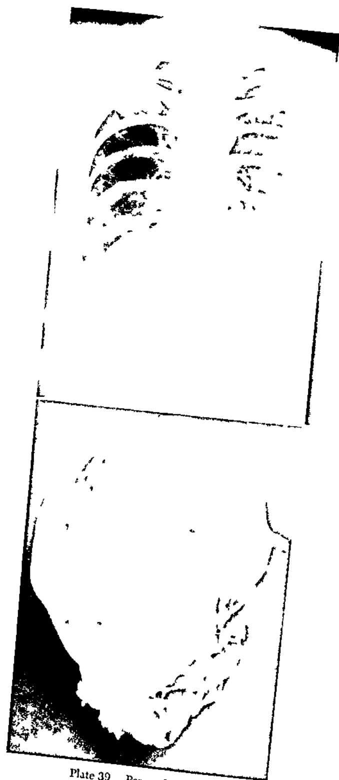


Plate 39 Pericardiophrenic Angle Cyst Celomic Cyst Mrs E A age 50
Fig 1 and 2 Smooth walled cyst at right base anteriorly
Fig 3 Specimen Thin walled pleural or celomic cyst



Plate 40 Aneurysm of Ascending Aorta J S, male, age 54

Fig 1 Luetic aneurysm

BENIGN TUMORS

Benign tumors of the sternum are the least common of the three types Chondroma or enchondroma are the most frequent At least one benign giant cell tumor of the sternum is recorded Local excision with reconstruction of the sternal area by fascial or bone graft or other prostheses have given good permanent results

MALIGNANT TUMORS

Primary malignant tumors of the sternum occur next in frequency to metastatic tumors As one would expect, some variety of sarcoma is the commonest type seen They usually cause pain and a local mass involving any portion of the sternum X ray studies will reveal an expanding type of tumor with destruction or alteration of the bony pattern of the sternum A diagnosis of malignancy should be suspected but often cannot be proved without biopsy. Treatment by radical excision of the sternum with reconstruction of the sternal area to stabilize the thoracic cage in this area would seem to be justified on a short-term basis but long-term results are likely to be found less frequently The effect of radiation therapy is quite unpredictable Rarely a plasma cell myeloma may present in the sternum as an apparently primary localized tumor and remain so for some time As myeloma is apparently a generalized process, local excision of such a local focus cannot be expected to give longtime results

METASTATIC TUMORS

Metastatic tumors occur most frequently, representing about 38% of reported series It is quite probable that they are considerably more frequent than are recorded in the literature because many cases with involvement by metastasis from carcinoma of the breast, carcinoma of the lung, malignant teratoma and others are never reported Among the commoner ones reported in the literature are carcinoma of the thyroid and carcinoma of the kidney, both of which may give a pulsating type of tumor in the sternum not encountered from other sources Metastases to the sternum from carcinoma of the breast carcinoma of the lung, and malignant teratoma of the mediastinum as well as malignant lymphoblastoma may occur and involve any portion of the sternum The results obtained by surgical excision of these metastatic tumors fails to justify the risk or the energy involved Radiation therapy in the lymphoblastoma group is of distinct value, but as a rule does not offer too much in the other types

INFLAMMATORY MASSES

Inflammatory masses in the sternum simulating tumor result from acute or chronic osteomyelitis, tuberculosis, eosinophilic granuloma and also occasionally from echinococcus cysts Careful examination will usually establish the inflammatory nature of the condi

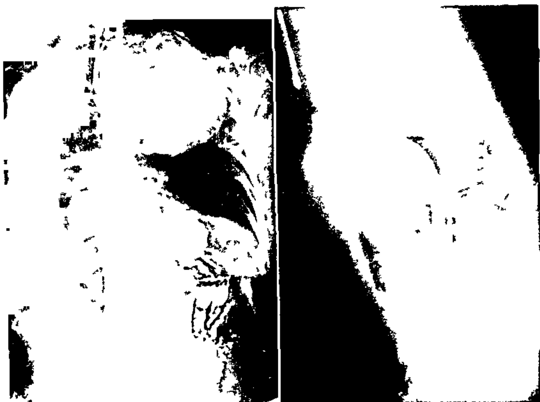


Plate 41 Aneurysm of Aorta R McC female age 58

Fig 1 and 2 Aortic aneurysm with calcium in wall Displacement of trachea and esophagus Serology negative Patient not arteriosclerotic or hypertensive Note calcium in wall of tumor

tion and differentiate it from tumor Local drainage and chemotherapy will control a number of these conditions but occasionally a local resection may be necessary

TUMORS OF THE DIAPHRAGM

Tumors of the diaphragm are extremely rare Scott and Morton in 1946 were able to collect only 33 primary tumors of the diaphragm from 1868 to 1946 In 1950 Sampson and Childress again reviewed the literature and added 2 cases of their own bringing the total up to 35 Half of the reported tumors were benign and half malignant Benign tumors reported included fibromas fibromyomas lipomas cysts hemangioendotheliomas angiofibromas lymphangiomas fibroangioendotheliomas and neurofibromas The malignant tumors were all sarcomas of a variety of types plus one hepatoma

Tumors of the diaphragm usually present as a large mass in the lower half of the chest and may reach huge proportions before discovery Pain may be present but more frequently the symptoms are related to the mass of the tumor and its pressure on the adjacent structures In one instance in a patient operated upon by the author a benign fibroma had a projecting nob of tumor which had inserted itself between the ribs and presented as a palpable mass in the lower axillary region on the right side This was truly an intrusion of the mass into the chest wall and not an invasion as that part of the tumor was shelled out very easily and no vascular or other attachments to the chest wall were noted When confronted with a



Plate 42 Subclavian Aneurysm Luetic Female 52

Fig 1 Aneurysm of subclavian artery Barium in esophagus Blood Wasserman positive Patient died from rupture of aneurysm

large mass in the lower chest the possibility of a diaphragmatic tumor must be considered The differential diagnosis must include eventration of the diaphragm diaphragmatic hernia (congenital or traumatic) encapsulated effusion huge chest wall tumor carcinoma of the lung an extruded basilar mediastinal tumor and metastatic tumor to lung or chest wall as well as a subdiaphragmatic tumor of liver or any of the upper abdominal organs

Barium visualization of the esophagus stomach and colon may be an aid in ruling out a *diaphragmatic hernia* *A diagnostic* pneumoperitoneum with air or oxygen will visualize the underside of the diaphragm if the subphrenic space is not obliterated and will help to rule out a tumor or an abscess of the liver Needle aspiration of the chest may be diagnostic if an encapsulated pleural effusion is suspected Diagnostic pneumothorax if the pleural cavity is not obliterated can separate the lung from the diaphragm thus ruling out the pulmonary mediastinal or chest wall origin of the mass X ray studies of the chest wall particularly for rib detail may give the answer if the tumor is of chest wall or bony origin

A bronchogram outlining the position of the lower and middle lobes on the right and the lower lobe on the left may also help in localization of the tumor Overexposed x ray films or planigrams may also help The demonstration of calcium in the region would be more suggestive of displaced teratoma than a tumor of diaphragmatic origin though it may occur in the latter if it is degenerating The density of the mass itself and its contour may give some suggestions as to the possibilities of a cyst or lipoma Irregularities of the barium filled esophagus may give some suggestion of a bronchial enteric or gastric cyst or other esophageal tumors which might be confused Needle biopsy may also give some information All of these studies might be of interest from an academic standpoint but if the patient's condition permits an exploratory thoracotomy will not only establish the diagnosis but at the same time will afford an opportunity for proper treatment

Resection of benign tumors and some of the malignant tumors will bring about cure A considerable portion of the diaphragm may be excised with the tumor and yet leave enough for adequate closure If direct closure cannot be obtained because too much has been sacrificed the diaphragm may be reconstructed using a sheet of fascia lata or some of the overlying ribs at the base may be resected and the chest wall brought in and approximated to the remaining portion of the diaphragm to permit adequate closure Results from excision of the benign tumors have been good Those from the removal of [illegible]

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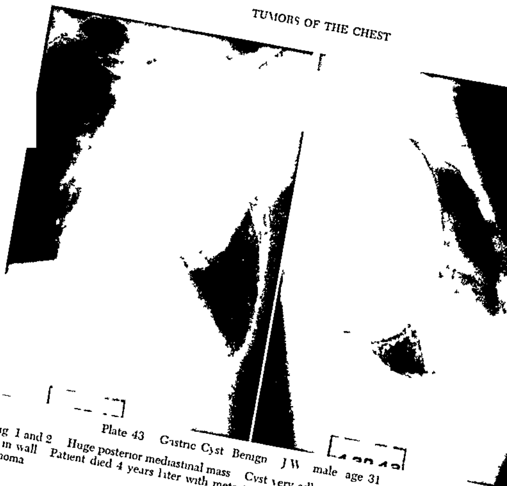


Plate 43 Gastric Cyst Benign J W male age 31

Fig 1 and 2 Huge posterior mediastinal mass Cyst very adherent thick walled with gastric mucosa in wall Patient died 4 years later with metastases to dorsal spine from primary bronchogenic carcinoma

carcinomas of the lung a few of the mediastinal tumors and benign fibrous mesothelioma of the lung have shown a dramatic improvement following removal of the tumor

TUMORS OF THE MEDIASTINUM

Tumors of the mediastinum should not only be considered under benign malignant and metastatic tumors and inflammatory lesions but they may also be subdivided into anterior and posterior mediastinal groups because such a division is of distinct help in recognizing preoperatively the type of tumor which may be encountered

Benign Tumors

Anterior	Posterior
Teratoma	Neurofibroma
Dermoid Cyst	Ganglioneuroma
Substernal Thyroid	Paraganglioma (Pheochromocytoma)
Pericardiophrenic Angle Cyst (Pleuropericardial Cyst)	Meningocele
Bronchial Cyst	Cyst Bronchial Gastric Enteric
Thymoma	Thyroid Adenoma
Lipoma	Tumors of Esophagus Leiomyoma Fibroma Lipoma
Parathyroid Tumor	Aneurysm of Aorta Traumatic
Aneurysm of Ductus Botalli	Chondroma



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ANTERIOR	POSTERIOR
Benign Tumors	
Teratoma	Neurofibroma
Dermoid Cyst	Ganglioneuroma
Substernal Thyroid	Paraganglioma (Pheochromocytoma)
Pericardiophrenic Angle Cyst (Pleuropericardial Cyst)	Meningocele
Bronchial Cyst	Cyst Bronchial
Thymoma	Gastric
Lipoma	Enteric
Parathyroid Tumor	Thyroid Adenoma
Aneurysm of Ductus Botalli	Tumors of Esophagus
	Leiomyoma
	Fibroma
	Lipoma
	Aneurysm of Aorta Traumatic
	Chondroma



Plate 44 Lipomyxosarcoma F K male age 20

Fig 1 Huge tumor displacing heart and mediastinum to right Dyspnea the only complaint Fifteen pound two ounce tumor removed Patient died from recurrence within the year

Anterior	Posterior
Malignant Tumors	
Lymphoblastoma	Carcinoma of Esophagus
Malignant Teratoma	Sarcoma
Leukemia	
Malignant Thymoma	

Metastatic Tumors

Bronchogenic Carcinoma
Carcinoma of the Breast
Carcinoma of the Stomach
Carcinoma of the Colon
Sarcoma

Pseudotumors

Pericardiophrenic Angle Fat Pad	Achalasia of Esophagus
Retrosternal Hernia (Foramen of Morgagni)	Hiatus Hernia
Traumatic Hernia	

Inflammatory Lesions

Tuberculous Lymph Nodes	Paravertebral Abscess
	Tuberculosis
Sarcoid	Staphylococcus
Aneurysm of Aorta	Brucellosis
Luetic	Mediastinal Abscess
Arteriosclerotic	
Tumors of the heart	

ANTERIOR MEDIASTINAL TUMORS

BENIGN

The commonest benign tumors encountered in the anterior mediastinum are the teratomas including the dermoid cyst followed by a substernal thyroid extension pericardiophrenic angle cyst (pleuropericardial cyst), benign thymomas and bronchial cysts The others are usually quite rare

Teratoma

Teratoid tumors of the mediastinum may occur at any age though they are recognized



Plate 45 Bronchial Cyst in Esophageal Wall Mrs W R age 54

Fig 1 2 and 3 Cyst in wall of midesophagus Smooth lumen outlined by barium Benig[n]
esophageal wall These cysts may usually be shelled out without entering the lumen of the es[ophagus]

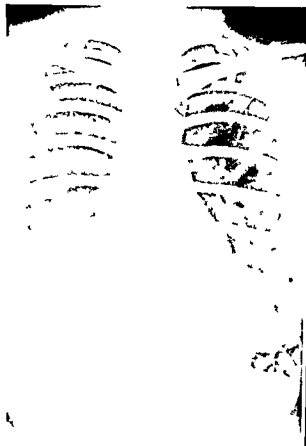





Plate 46 ma W K

Fig 1 and chest r an

d 4



Fig 5 Benign leiomyoma and resected segment of esophagus Reconstruction by esophagogastrostomy

less commonly in children than in adults They usually develop in the midline but may project more to one side than the other and rarely may be extruded from the mediastinum on a stalk carrying the blood supply to indicate their point of origin While frequently of somewhat nodular or irregular shape they may be perfectly smooth and regular and globular in contour The size may vary widely from a small one (up to 3 cm in diameter) which may hide behind the sternum and be unrecognized unless lateral films are taken to a huge mass which may fill a major portion of the thorax They may be cystic or solid in character or a combination of both The composition varies greatly from the simple dermoid cyst containing only sebaceous material through the more complicated dermoid containing sebaceous material hair skin and teeth to the extremely complex teratoid tumor containing structures from all three germinal layers to the extremely complex fetal parasite" containing bits of almost all tissues and structures of the body

They may be rather loosely attached in the mediastinal tissues or densely attached with scar tissue exceeding 1 cm in thickness The attachments to pericardium vessels trachea or bronchi may be extremely dense Not infrequently finger like projections extend out around or between the adjacent structures They may remain static in size for long periods of time or may grow very rapidly While any increase in size should always make one fearful of malignant change it can occur in perfectly benign tumors, from simple growth hemorrhage or an increase in secretion in a cystic portion of the mass

Many of these tumors produce no symptoms for long periods of time Others though smaller may produce symptoms by pressure or irritation from attachment to adjacent projects Sooner or later however the majority produce symptoms in one of four ways by increase in size pressing upon and displacing other structures by becoming adherent to adjacent trachea, bronchus or lung with perforation the patient expectorating greasy ma



Plate 47 Leiomyoma of the Esophagus S S male age 35

Fig 1 and 2 Tumor right base in midchest on lateral film

Fig 3 and 4 Barium esophagram Ulcer in tumor area Removed through a combined anterior intercostal sternal splitting and midline upper abdominal incision Esophagogastrostomy



Plate 48 Rhabdomyoma of the Heart S L J female age 8 weeks

Fig 1 Huge heart shadow Patient died at 8 weeks

terial or hair in the sputum by becoming infected the patient becoming septic and perhaps having the mass drained as a mediastinal abscess or empyema or by undergoing malignant change with direct invasion of adjacent chest wall or pericardium or heart or metastatic spread Because of these complications it is the consensus of opinion of thoracic surgeons that all mediastinal teratomas should be surgically removed preferably before they begin to cause trouble

The x ray picture of an anterior mediastinal teratoma is not always diagnostic If one plays the percentages and calls every localized completely anterior mediastinal mass a teratoma one would be correct about 75% of the time If the overexposed x ray films or planigrams demonstrate the presence of teeth or bone the diagnosis then becomes quite certain The demonstration of calcium alone is not so conclusive as it occurs frequently in substernal thyroid tumors some aneurysms and in some thymic tumors particularly if there has been necrosis and hemorrhage within the tumor mass

Substernal Thyroid

Thyroid adenomas developing in the inferior or posterior parts of the gland particularly in the broad chested rather heavily muscled types of individuals have a tendency to extend downward and present as upper mediastinal tumors usually anteriorly but occasionally between the trachea and esophagus and more rarely posteriorly The possibility of such a condition must always be considered whenever one is confronted with a superior mediastinal shadow particularly if the shadow extends upwards to the level of the clavicles Occa

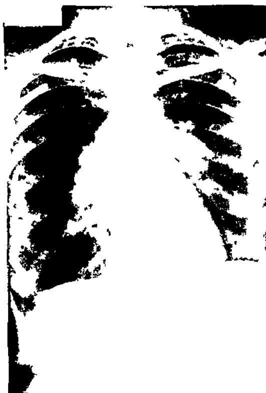


Plate 49 Boeck s Sarcoid Mrs M F, age 38

Fig 1 Bilateral parenchymal infiltration and mediastinal lymph node enlargement



Plate 50 Tuberculous Mediastinal Lymphadenitis P W male age 14

Fig 1 and 2 Enlarged and calcified mediastinal lymphadenitis as part of extensive tuberculous disease of cervical axillary and mediastinal nodes Mediastinal vascular obstruction Improved under anti tuberculosis therapy

sionally there may be a history of a previous goiter which has disappeared or has been surgically removed Not infrequently the upper margin of the mass may be palpable in the neck and may be felt to elevate upon swallowing Rarely a bruit or thrill over the lower thyroid vessels may be found The patient may be entirely asymptomatic but may though frequently does not present symptoms of hyperthyroidism He may have cough stridor dysphagia or vascular obstruction in the head neck and upper extremities on one or both sides from pressure of the mass in the mediastinum

Voice changes from interruption of laryngeal nerves and cord paralysis may occur but is rather rare in the benign tumors being more common when malignant change has occurred Deviation of the trachea with suffusion and cyanosis of the face arms and upper extremities possibly with edema (superior vena caval obstruction syndrome) may be the presenting physical findings From the x ray standpoint an upper mediastinal mass with compression or deviation of the trachea is the most common finding Thyroid tumor or aortic aneurysm are most likely to produce tracheal deviations or compression The presence of calcium in the mass on x ray film is quite characteristic if hemorrhage and degeneration has occurred within the adenoma Fluoroscopic demonstration of elevation of the mass on swallowing is quite characteristic

Visualization of the esophagus with a barium mixture not infrequently will show a projection of the thyroid tumor between the trachea and esophagus displacing the one anteriorly and the other posteriorly as well as producing lateral deviation The presence of lateral compression of the trachea should call attention to



Plate 51 Lymposarcoma of Med astinum R C male age 32

Fig 1 3 12-45 Mid mediastinal tumor
F g 2 4 14-45 Recession of tumor follo ving x ray rad ation Pat ent d ed from recurrence of tumor 9 months later

the possibility of bilateral tumor masses of thy roid origin or to an encircling type of tumor Radioactive iodine uptake studies or localiza tion of such concentration in the tumor mass as demonstrated by the scintillometer or Geiger counter may establish a definite diagnosis

Substernal thyroid tumor mass should be re moved surgically The general tendency is for the masses to increase in size with slowly increasing pressure symptoms Rapid increase in size from growth or from sudden hemor rhage into a degenerating adenoma may pro duce an alarming increase in obstructive symptoms and may prove fatal The possi bilities of malignant change within the sub sternal mass must always be remembered

From a surgical standpoint it is well to remember that the vast majority of these tumors originate in the neck and as they de scend into the chest carry with them the blood supply from the inferior thyroid vessels Rarely a parasitic blood supply develops in the mediastinum particularly if degeneration or malignant change has occurred The ma jority of these tumors with some notable ex ceptions may when their upper attachments have been freed be removed from above through the usual collar incision particularly if intratracheal anesthesia is utilized to main tain an open airway Some if rather large and bulbous below may have their mass re duced by opening the capsule above and morselating the tumor to reduce the size of the mass and permit its extraction through the superior strait of the thorax A few large tumors will require a vertical splitting of the sternum in addition to the ordinary collar incision for successful removal There are a few posteriorly located thyroid adenomata which may require a posterior thoracic ap-

proach but the blood supply will usually be found to come from above Rarely a thyroid tumor a true aberrant thyroid not connected with the thyroid above may occur and its removal requires transthoracic approach or a more extensive sternal splitting incision

Pericardiophrenic Angle Cyst (Pleuropericardial or Celomic Cyst)

Not uncommonly particularly on routine survey chest x ray films a rounded shadow is observed in the angle between the pericardium diaphragm and the anterior chest wall The density is usually not great the contour is smooth and at times the lower end of the shadow can be separated from the diaphragm on deep inspiration but in others this cannot be demonstrated There are three conditions which commonly produce such a picture The commonest is an exaggeration of the normal pericardiophrenic angle fat pad which lies in this position The second is a cyst filled with crystal clear fluid adjacent to and at times closely associated with the pericardium with which occasionally it may communicate The pleuropericardial cyst (celomic cyst) is often called a pericardiophrenic angle cyst The third condition is a retrosternal hernia through the foramen of Morgagni The pericardiophrenic angle fat pad and retrosternal hernia will be discussed under pseudotumors They rarely if ever produce symptoms except perhaps those of psychogenic origin in the patient who has discovered that he has a shadow in the region of his heart Surgical removal of a cyst in this location is easily accomplished through an anterior thoracotomy incision If the cyst communicates with the pericardium it can be excised and the pericardial opening sutured If one can be fairly certain of the diagnosis beforehand and usually this is so there is usually no surgical indication for removal of the cyst

Thymoma

Benign tumors of the thymus may be either solid or cystic Both present as rounded completely anterior tumor masses projecting to one side or the other of the sternum and lying at any level from the clavicle to the diaphragm The patients are almost entirely asymptomatic The tumor mass usually is discovered on a routine x ray film of some sort The hypertrophied thymus shadow of infants rarely produces the symptoms for which it is blamed Cystic degeneration in the region of the thymus may be of celomic origin (spring water cyst), but may be called thymic at times by courtesy of its position rather than from the microscopic picture The association of thymic tumor with myasthenia gravis is still the subject of much controversy as are the results obtained from surgical removal of thymic tumors of the thymus itself for this condition

The surgical removal of thymic tumors and thymic cysts is rather easily accomplished by anterolateral or anterior thoracotomy incision or through a sternal splitting incision Complete removal of the thymus and its extensions which at times have the contour of the letter "H" is somewhat more tedious but can be accomplished with greater facility through a transverse sternal splitting incision

Bronchial Cysts

Cystic structures of varying sizes containing a wall which shows a microscopic picture of bronchial mucosa may occur on either side and at almost any level of the anterior of mid mediastinum They may lie in close approximation to the trachea or one of the major bronchi but may be completely free from such attachments and have no physical connection with the lung trachea or bronchial tree The cysts are rounded to ovoid in character lie underneath the mediastinal pleura and contain fluid which is clear to slightly cloudy usually having a wall which is slightly opaque or is very thin and clear, permitting transillumination without difficulty These cysts may produce no symptoms and are usually discovered accidentally Occasionally one may reach such huge size that pressure symptoms develop Surgical removal is usually readily accomplished by shelling out the cyst from the mediastinum though occasionally the attachments to bronchus or trachea are quite dense and require careful dissection to avoid entering the tracheal or bronchial wall

Lipoma

Fatty accumulations are seen quite commonly in the mediastinum particularly in patients of good nutrition but very rarely a true lipoma may be encountered presenting as a tumor mass It may attain huge size and not infrequently show finger like projections which extend around or between other mediastinal structures Quite a few of them have a dumbbell character with part of the tumor presenting in the neck or chest wall as well as in the mediastinum Some of the largest tumors encountered within the thorax fall into this group Surgical removal is usually possible but it may be somewhat tedious because of large size and the extension of the tumor around other structures

Parathyroid Tumors

Tumors of parathyroid origin rarely present as a tumor mass or attain a size which can be recognized on x ray films The occasional patient presenting the clinical picture of hyperparathyroidism with serious disturbance of calcium metabolism and in whom a thorough search of the cervical region and the region behind the thyroid has not revealed the offending tumor may require exploration of the mediastinum in a search for it Such tumors may lie in the anterior mediastinum and may even be imbedded in the substance of the thymus gland Exploration of the anterior mediastinum through an anterior thoracotomy incision or through a transverse sternal splitting incision may be worthwhile At times it is necessary to excise the entire thymus gland in a search for the offending mass

Aneurysm of the Ductus Botalli

There is a rare anterior mediastinal tumor mass encountered on the left side in the normal individual or on the right side in the case of situs inversus which is spherical frequently pulsatile in nature arising as an aneurysmal dilatation of the patent ductus arteriosus The clinical picture of a patent ductus arteriosus plus a pulsating anterior mediastinal shadow should establish the diagnosis Excision of the aneurysmal sac with suture of the pulmonary artery and the aorta may be carried out successfully

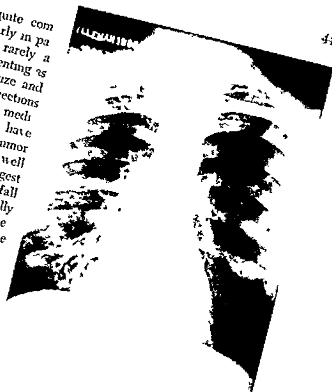


Plate 52 Isolated nodule—not pulmonary W T male age 50

Fig 1 Pigmented mole on back simulates isolated pulmonary nodule right third interspace Nipple shadows sebaceous cysts, a thumb or something in or on clothing may simulate a pulmonary nodule on the single film

MALIGNANT TUMORS

Lymphoblastoma

Lymphoblastoma of either the Hodgkins or the lymphosarcoma type usually are of mediastinal origin in the lymph node bearing area but not infrequently present as a mass which extends well anteriorly as seen on the lateral chest film If associated with other lymph node involvement in the mediastinum cervical region or elsewhere the diagnosis may be easily made If the mass presents largely in an anterior mediastinal position with no



Plate 53 Isolated Pulmonary Nodule Granuloma Mrs H C age 37

Fig 1 and 2 Granuloma of tuberculosis

other indication of lymphatic enlargement the problem of differential diagnosis may be somewhat complicated If the mass is not large and yet mediastinal vascular obstruction is present the possibility of a lymphoblastoma must be seriously considered because it is an invasive process and the other types of smaller anterior mediastinal masses usually do not produce such obstruction Chylothorax and chylous ascites occur more commonly with lymphoblastoma than with any other mediastinal lesion

Complete blood studies to rule out leukemia a search for available lymph nodes for biopsy including biopsy of the lymph nodes in the fat pad over the scalenus anterior muscle and in the superior mediastinum on both sides plus a bone marrow biopsy may be tried in an attempt to establish a definite diagnosis Failing in these procedures diagnostic therapeutic test of x radiation or nitrogen mustard administration may be used as a diagnostic method The nodular character of the ordinary mediastinal lymphoblastoma with the presence of the mass in the node bearing area and the bilateral lymph node enlargement are of help in differentiating this condition from the ordinary mediastinal tumors

Occasionally the infiltration of Hodgkins disease will involve the bronchus producing bronchial obstruction and the clinical picture of bronchogenic carcinoma in which case bronchial biopsy may establish the diagnosis The clinical finding of skin lesions or an intense pruritus may occasionally give the clue to the correct diagnosis in lymphoblastoma of the Hodgkins type Occasionally an isolated tumor mass may be found in the hilar region which resembles a lung tumor rather than a mediastinal tumor The very slow progress of such a lesion may easily lead one astray It is well to remember that Hodgkins disease



Plate 54 Isolated Pulmonary Nodule Granuloma

Fig 1 Nodule right lower lung field W F male age 55

Fig 2 Concentric ring granuloma of histoplasmosis Specimen

may run a very prolonged course both with and without treatment Surgery has little to offer in this type of condition It is only rarely that such a mass presents itself as suitable for surgical excision the process usually being diffuse and infiltrative The response to radiation or to nitrogen mustard injection is at times quite spectacular on a temporary basis but recurrences are the rule rather than the exception Not infrequently the more rapid the response the more quickly the process returns locally or elsewhere Occasionally this condition especially the Hodgkin's type may run a very prolonged course with survivals of 5 or 10 to 20 years occasionally recorded

Malignant Teratoma

Malignant degeneration in a teratomatous tumor in the mediastinum is encountered in roughly 15% of cases Whether the process has been malignant from the start or whether it represents a malignant degeneration of certain elements within the composite mass is uncertain though in some the latter would appear to be true because of the long duration of the mass before rapid growth started A rapid increase in size of a previously stable tumor always raises the question of malignant degeneration Malignant degeneration rarely becomes clinically diagnosable until invasion of adjacent structures has occurred Theoretically surgical excision would be the procedure of choice but what good results have been obtained by such treatment have usually occurred where the tumor was still definitely encapsulated and unrecognizable grossly as a malignant process the diagnosis being made on microscopic examination after the successful removal of a localized noninvasive tumor Where such malignancy has occurred with in

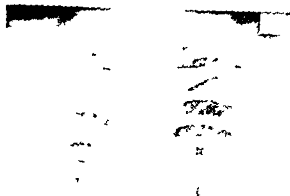


Plate 55 Isolated Pulmonary Nodule *Granuloma* Mrs W age 59

Fig 1 Isolated pulmonary nodule—coccidiomycosis Resected

vasion locally surgery probably has little to offer Direct extension of the tumor to adjacent pericardium heart lung and other mediastinal structures as well as lymphatic extension distant metastasis and chest wall invasion may occur

Thymoma

Malignant thymoma is one of the conditions we must always bear in mind when confronted with an anterior mediastinal tumor particularly in the younger individual It may occur at any level of the mediastinum and frequently is not as sharply outlined as the teratomas or cysts and not as dense as seen on the x ray film Early it may be sharply encapsulated and offer some hope of surgical excision but later it tends to infiltrate locally into adjacent structures into the mediastinal lymphatics and later into the chest wall Distant metastases tend to occur rather late with liver involvement in about one fifth of the patients Mediastinal vascular obstruction and involvement of cervical lymph nodes may be one of the early indications of a malignant thymic tumor Once local invasion has begun surgery has little to offer in this type of tumor Radiation therapy may give a very favorable result temporarily but recurrence is the rule

Leukemia

Occasionally a leukemic infiltration may present as a localized mediastinal tumor similar to the lymphoblastomas Blood and bone marrow biopsy studies as well as lymph node biopsy will establish the diagnosis If the mass or tumor is producing obstruction radiation therapy may give temporary relief

Liposarcoma or Lipomyxosarcoma

Malignant change of a sarcomatous nature in a mediastinal lipoma or myxosarcomatous change may occasionally be encountered These tumors may be huge in size and even reach ten to fifteen pounds in weight producing marked displacement or obstruction Complete surgical removal usually is impossible The response to radiation is unsatisfactory

METASTATIC TUMORS

Metastatic invasion of the mediastinum is usually through the lymphatics but occasionally by direct extension It occurs most commonly from primary bronchogenic carcinoma but may be encountered in carcinoma of the breast stomach or colon or sarcoma elsewhere in the body Masses of huge size may result with obstruction of the superior vena cava giving the characteristic superior vena caval syndrome of dilated veins suffusion of the face cyanosis of the upper extremities neck and head and edema of the same structures The lymphatic masses may gradually produce tracheal bronchial or esophageal obstruction Occasionally they produce lymphatic obstruction and chylothorax If the primary tumor in the lung is small and not readily seen or if an extrathoracic primary is not evident the mediastinal involvement may cause confusion for a

time as to its exact etiology The surgeon has nothing to offer in this group of patients Radiation therapy may produce temporary relief at times for several months The eventual prognosis is not good

INFLAMMATORY MASSES

Aneurysm

Aneurysms of the aorta either luetic or arteriosclerotic in origin may present a very confusing picture in the mediastinum If such a mass presents a characteristic picture of thrill bruit heart murmur or pressure changes between the two arms and displacement of the trachea with paralysis of the left vocal cord the diagnosis becomes simple especially if a positive serology report is on the chart If at the same time the mass produces tracheal displacement and shows expansible pulsation on fluoroscopic observation or on roentgenkymograms the diagnosis is easy Frequently however such a characteristic picture is not encountered The aneurysmal sac may be filled with a laminated clot with no pulsation to be seen and no bruit or thrill to be demonstrated The presence of linear calcium deposits in or around the mass may be a definite aid in diagnosis Variations in the pulse and the blood pressure in the two arms and deviation of the trachea and esophagus may help in localization and thus establish the diagnosis

The somewhat spindle shaped to ovoid right paravertebral shadow of an innominate artery aneurysm can be easily confused with a neurogenic tumor or a carcinoma developing in the apical posterior segment of an upper lobe on the ordinary chest film The lateral film may help greatly in the differential diagnosis Numerous good results are now appearing in the literature following surgical excision of aneurysms with reconstruction by aortic graft or other types of prosthesis

Tuberculous Mediastinal Lymphadenitis

This was once a common condition particularly in young children following primary tuberculous infection especially of the bovine type with the development of huge masses of tuberculous lymph nodes in the mediastinum



Plate 56 Isolated Pulmonary Nodule Pulmonary Cyst V O female age 36

Fig 1 Isolated pulmonary nodule right base posteriorly Benign pulmonary cyst

with or without accompanying cervical lymphadenitis Such conditions are rarely seen now except occasionally among the Indians and some of the darker skinned races A history of exposure to tuberculosis a positive Mantoux test the nodular character of the mass and its bilateral distribution and the association with cervical nodes available for biopsy and later the presence of calcification in the lymph node masses usually made the diagnosis relatively easy The response of these nodes to x ray in the earlier stages was quite gratifying Now treatment with anti tuberculosis drugs offers far more for the patient who presents such a condition

Boeck s Sarcoid

Sarcoid of the mediastinum is now being seen or at least recognized with increasing fre

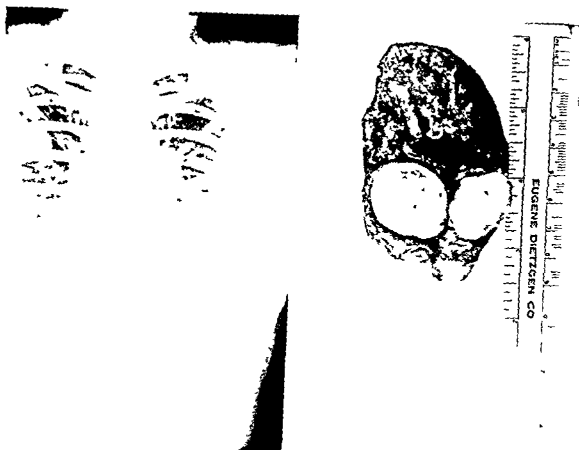


Plate 57 Isolated Pulmonary Nodule Fibroma Mesothelioma Benign D N, female age 18
Fig 1 Local nodule right second interspace
Fig 2 Specimen

quency The nodular character of the mediastinal shadow, its bilateral distribution and frequency of right paratracheal lymph node enlargement, plus the frequent occurrence of parenchymal infiltration bilaterally should suggest the diagnosis The most accurate way to confirm the clinical diagnosis lies in examination of lymph node biopsy material particularly that obtained by dissection of the scalene fat pad and upper mediastinum through a cervical approach Probably the highest percentage of positive results from scalene lymph node biopsies are found in sarcoid The Kveim skin test has not proven particularly reliable in many hands, although some favor it The process is not infrequently ushered in by an episode in malaise, suggestive of an infection the nature of which is absolutely unknown Very often it runs a rather prolonged course, is usually benign but occasionally progressively fatal. There is no successful treatment for it

PSEUDOTUMORS OF THE ANTERIOR MEDIASTINUM

One of the commonest abnormal anterior mediastinal shadows presented to the thoracic surgeon for consideration is a rounded or slightly lobulated shadow lying anteriorly in the pericardiophrenic angle This shadow is usually representative of one of three things the commonest, an unusually large accumulation of fat in the pericardiophrenic angle fat pad the next, the pericardiophrenic angle cyst or celomic cyst (pleuropericardial cyst), and third, hernia through the retrosternal diaphragmatic defect (Foramen of Morgagni) A number of this latter group contain only extraperitoneal fat, though a few contain omentum intestine or colon If intestine is present in the hernia, the presence of a gas bubble on the x ray film easily identify it. A diagnostic pneumoperitoneum will easily identify the sac if it is freely communicating with the perito-

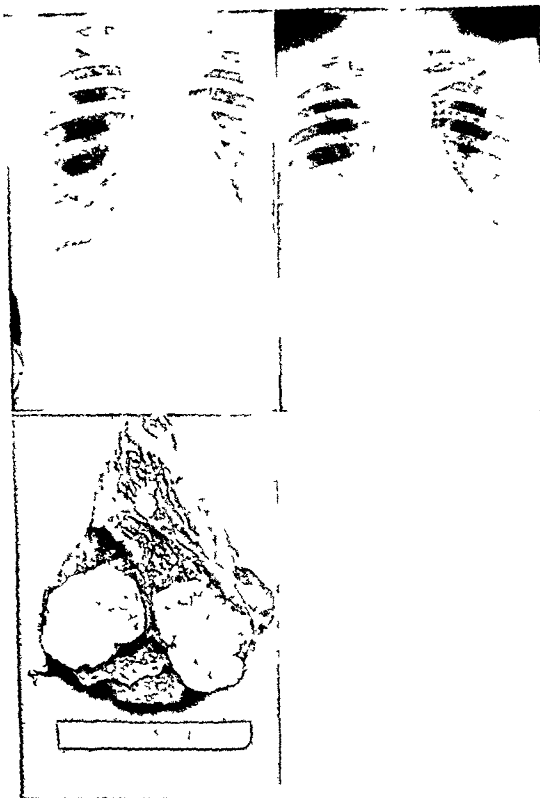


Plate 58 Isolated Pulmonary Nodule Chondromatous Hamartoma B H female age 57



Plate 59 Isolated Pulmonary Nodule Chondromatous Hamartoma C S S male age 40

Fig 1 Hamartoma with irregular calcium deposits right base
Fig 2 Detail

neal cavity X ray visualization of the stomach intestine or colon outlined by barium will easily prove the nature of the contents If the hernia contains only extraperitoneal fat as it most frequently does the diagnostic pneumoperitoneum will be of no help

Neither the herniated fat the pericardiophrenic angle fat pad nor the pericardiophrenic angle cyst do the patient any particular harm As there are no lesions of serious type which commonly occupy this position they may with safety be considered nonsurgical These constitute the only group of thoracic masses which can with almost 100% certainty be passed up and not treated surgically The true hernias containing intestine stomach or colon should of course be surgically repaired Rarely a traumatic diaphragmatic hernia may occupy this extreme anterior position This of course should be surgically repaired as the herniated structures are frequently adherent and strangulation is always a real danger A transthoracic approach offers best exposure for dealing with structures adherent about the diaphragmatic tear

POSTERIOR MEDIASTINAL TUMORS

Neurofibroma, Ganglioneuroma

The most frequently encountered tumor mass in the posterior half of the chest is the fibrous tissue tumor of neurogenic origin neurofibroma or ganglioneuroma Although frequently called posterior mediastinal tumors, they are truely of chest wall origin and have been previously discussed as such



Plate 60 Isolated Pulmonary Nodule Arteriovenous Fistula of Lung C B female age 25

Fig 1 and 2 Tumor with incoming vessels from hilum

Fig 3 Specimen Apical and posterior segments injected with lipiodol and x rayed Artery below and vein above

Meningocele

The possibility of an intrathoracic meningocele must always be considered when confronted by a spherical, ovoid or tear-drop shaped mass lying in the vertebral gutter adjacent to the lateral foramina. The density of the shadow should be slightly less than that of the solid tumors with a tendency toward a water bottle shape. There may be, but usually is not, any suggestion of any cord disturbance. If the condition is suspected, a *diminution in size following spinal tap might help to establish the diagnosis.* Usually it is not made preoperatively.

In the operating field the cystic nature of the mass, its ready transillumination and its position should certainly make one suspect a meningocele. Its surgical removal must be done carefully, preserving any nerve elements that may be present in the wall of the sac and also saving enough of the wall of the sac to permit an adequate closure of the dura to avoid post operative spinal fluid leakage.

Chondroma

Very rarely a chondroma may develop posteriorly, taking its origin from the intervertebral disc, from the articular facets of rib or vertebral body, or directly from either of these structures. The condition is so rare that the preoperative diagnosis is usually not made unless the presence of calcium or bone is demonstrated on the preoperative x-ray to give the clue to the true nature of the condition. Complete removal of such tumors may not be possible depending upon the structure involved and the nature of attachment. In this case recurrence may be expected occasionally even without malignancy being present.

hypertension during manipulation of the tumor and the hypotension that may follow its removal.

Cyst

Reduplication cysts or cysts of bronchial, enteric or gastric origin may occur within the chest more commonly posteriorly than anteriorly and may lie at any level in the thorax. It may be possible to recognize the cystic nature of the mass preoperatively but frequently it is not. If perchance a diagnostic aspiration has been carried out, which is not recommended, the aspirated material should be studied in the laboratory for hydrochloric acid and for enzymes which may give a clue to the nature of the presenting mass.

In the operative field some may be thin walled and transilluminate easily, but others may be relatively thick walled with cloudy contents and will not transilluminate. If the cyst is ruptured in its removal the contents should be saved for laboratory study. The final diagnosis usually rests upon microscopic examination of the cyst wall. Characteristic sections resemble normal bronchial wall, small intestinal wall or the stomach, with all tissues in good orientation, at times even with a secreting mucosa identified. No malignant degeneration of such rests has been reported to our present knowledge.

Tumors of the Esophagus

Tumors of the esophagus, of which carcinoma is by far the most frequent, usually do not present a mass which can be confused with other mediastinal tumors. Occasionally, however, carcinoma of the esophagus will present a mass which protrudes laterally as a mediastinal mass. A history of dysphagia, the esophagram and esophagoscopic examination will readily make the correct diagnosis.

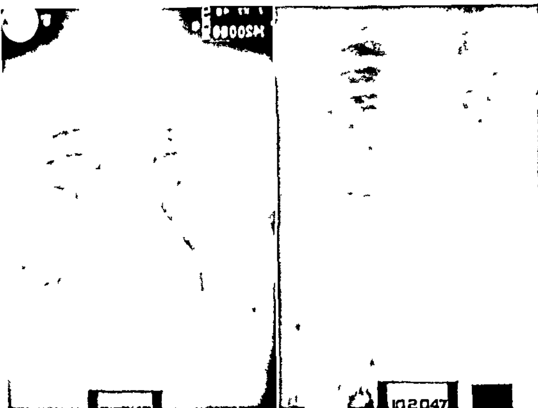


Plate 61 Isolated Pulmonary Nodule Primary Bronchogenic Carcinoma Squamous Cell W H female age 56

Fig 1 7 27 45 Isolated nodule Positive Mantoux Treated for tuberculosis
Fig 2 10 20-47 Bronchogenic carcinoma with metastases

broadening of the mediastinum or a localized bulging to the right particularly in the lower portion The lateral chest film the presence of a fluid level or the esophagram will soon make the proper diagnosis

The relatively rare bronchogenic cyst in the esophageal wall may present as a smooth localized mediastinal bulge usually on the right side Its midthoracic position on the lateral x ray film will quickly call attention to its possible origin The esophagram gives a typical picture of a smooth indentation of the esophageal lumen with an intact mucosa with the tumor mass outlined adjacent to it Some of these cysts are covered by esophageal musculature while others show only an occasional strand of muscle or a few fibrous bands overlying them laterally These do not as a rule have any communication with the esophageal lumen and can usually be shelled out without entering the lumen of the esophagus and with preservation of the majority of the esophageal muscle fibres These cysts are usually thin walled containing a thin fluid which is clear or only slightly cloudy The microscopic picture of the wall is that of bronchial mucosa of a benign type

A localized pulsion or traction diverticula of the esophagus if filled with food may at times present as a small mass though ordinarily a fluid level will be the give away as to the nature of the condition and the esophagram will easily confirm it Rarely a huge pharyngeal (pharyngeo-esophageal) or Zenker's diverticulum projects down into the upper mediastinum On x ray film this presents as a mediastinal shadow The history of dysphagia

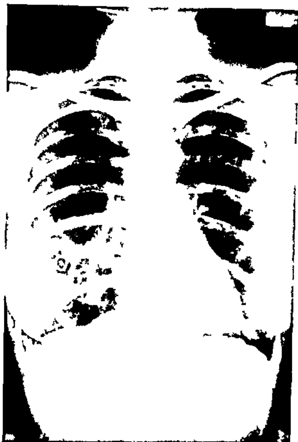


Plate 62 Isolated Pulmonary Nodule Adenocarcinoma Primary Mrs R A J age 50

Fig 1 Nodule right base The nipple is marked by paper clip Eighteen months history Resected Died 4 years later from recurrence

with regurgitation and the esophagram will usually establish the true diagnosis

Aneurysm of the Aorta

Traumatic aneurysm of the aorta mycotic aneurysm of the aorta and arteriosclerotic or dissecting aneurysm may present as a posteriorly situated tumor which may be confused with some of the other mediastinal masses The demonstration of an expansile pulsation may be a great help in differential diagnosis but is frequently not seen in aneurysm A history of trauma the presence of back pain or a bruit or thrill may aid in differential diagnosis The localized type of aneurysmal dilatations may now be surgically repaired by excision suture or by the insertion of a graft

Hiatus Hernia

The possibility of a hiatus hernia must always be considered particularly when an abnormal shadow is demonstrated behind the heart Its central location on the lateral chest film and the presence of a gas bubble and fluid level will frequently establish the diagnosis which is easily confirmed by a barium study of the esophagus and stomach Traumatic diaphragmatic hernias may occur in any situation on either side of the chest and in any position in the diaphragm Those which permit the passage of hollow viscera into the chest are rather easily diagnosed by x ray or barium study Those which contain only spleen or omentum are less easily differentiated A diagnostic pneumoperitoneum may be of considerable help An accurately taken history may be very important Very rarely one may encounter a small area of subphrenic or perirenal fat herniation through a very small defect in the diaphragm presenting as a sharply circumscribed rounded mass of moderate density moving with the diaphragm on respiration The opening through the diaphragm is usually small and easily repaired after excision of the protruding fat

Paravertebral Abscess

Paravertebral abscess from tuberculosis of the spine staphylococcus osteomyelitis or brucellosis of the dorsal spine occasionally may show on the x ray film as a rounded or oval paravertebral shadow which may simulate a posterior mediastinal tumor The pain muscle spasm knuckle deformity and x ray evidence of spinal caries or vertebral wedging will easily suggest the true diagnosis

Mediastinitis

Mediastinal infection once a serious and often fatal condition is now less commonly seen and less to be feared thanks to modern chemotherapy Contrary to the older impressions that the mediastinum was very vulnerable to contamination later experience has shown that it is really quite resistant to infection and may localize and tolerate it quite well

The commonest source of mediastinal infection is some lesion of the esophagus for

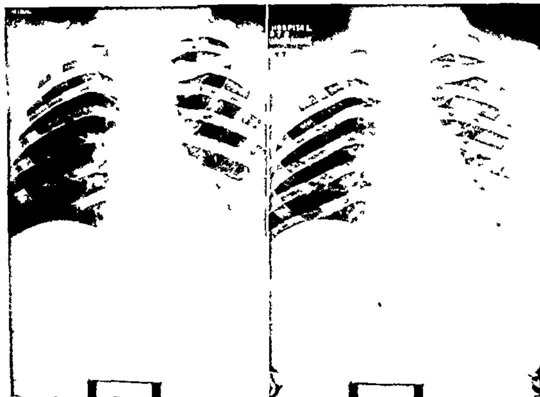


Plate 63 Isolated Pulmonary Nodule Metastatic Carcinoma Breast to Lung Mrs W N age 42

Fig 1 and 2 Slow growth of metastatic tumor in 16 months Right radical mastectomy 9 years before Left upper lobectomy Patient survived 4 years

eign body perforation perforation of a diverticulum instrument perforation spontaneous perforation or erosion of an esophageal carcinoma Before the days of chemotherapy and antibiotics such contamination was of serious import and even if surgical drainage was instituted promptly the mortality rate was fairly high Modern chemotherapy has materially changed this picture for while early surgical drainage of the local area is still indicated the chance of recovery has vastly improved

Foreign body perforation of the cervical esophagus if large or not seen early in addition to chemotherapy requires drainage of the local site the upper mediastinum on the same side and perhaps bilaterally The smaller perforations may be treated by antibiotics alone if food is withheld Perforations in the thorax may require a posterior mediastinotomy

Direct perforation from esophagoscopy or dilatation or perforation of a diverticulum should be operated upon at once and the defect sutured Spontaneous perforation of the esophagus to the mediastinum and secondarily to the pleura should be operated upon at once not waiting for the patient's condition to improve The tension pneumothorax must be relieved the food and acid removed from the pleural cavity and the mediastinum the esophageal rent sutured and the mediastinum and pleural cavity drained A feeding tube should be inserted and intensive chemotherapy instituted Erosion of an esophageal carcinoma into the mediastinum with perforation usually occurs late and offers little hope for surgical relief

Perforation of the esophagus from dilatation if not extensive and not followed by progressive emphysema may well be treated conservatively by antibiotics no food or drink by

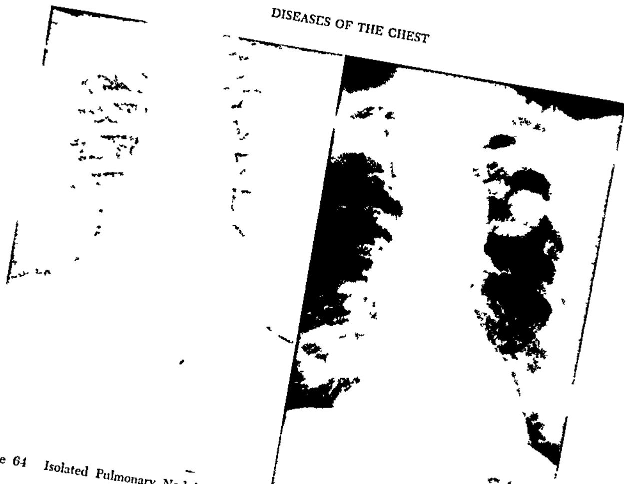


Plate 64. Isolated Pulmonary Nodule — Metastatic Carcinoma from Carcinoma of Small Intestine.

Fig. 1 and 2. A. M., male, age 77. Increase of tumor in 6 weeks. Resected metastatic carcinoma, site undetermined. Intestinal obstruction 6 months later and primary then found.

mouth and a nasal tube for feeding. The larger perforations should be operated upon promptly, the rent closed and the mediastinum and pleura drained.

Rarely a chronic mediastinitis developes from a suppurating lymph node, tuberculous or non-tuberculous, an infected or leaking dermoid cyst or a peri-esophagitis with the production of very dense scar with or without small abscess formation. This condition will usually not be mistaken for tumor and not be recognized except at surgical exploration.

TUMORS OF THE HEART

Primary tumors of the heart occur very rarely. Mahaim collected some 300 cases from the published literature and reported that 100, or approximately one third, were myxomas. Most of these were located in the left atrium and many of them were found only on post mortem examination. Fibromyxoma, rhabdomyoma, modified fibroma (benign fibrous mesothelioma), lymphangioendothelioma, hemangioendothelioma and hamartoma have been reported. An appreciable incidence of sudden deaths is to be noted in the reported cases. Primary malignant tumors are almost as rare. Sarcoma, lymphosarcoma, fibrosarcoma, leiomyosarcoma and rhabdomyosarcoma have been reported. Sudden death likewise is not infrequent in this group but apparently occurs less commonly than in the benign tumors.

Metastatic involvement of the heart, on the other hand, is not at all infrequent Bisel, Wroblewski and LaDue reported 21% involvement from a series of 500 consecutive autopsies on patients dying of neoplastic disease Cardiac involvement was reported in 44% of those dying of leukemia, 44% of those dying of malignant melanoma, 33% of those dying from breast cancer 31% of those dying from carcinoma of the lung and in 24% of those dying from lymphoma The pericardium was involved in 5 7% of the leukemic group and 49 4% of the remainder Cardiac metastases were always associated with wide spread metastases to many other organs Electrocardiographic findings were reported as suggestive but not diagnostic in 28% of the patients with cardiac metastasis The possibility of cardiac tumor, primary or metastatic, may be suggested by intractible cardiac dysfunction in the absence of an obvious cause, extreme unexplained cardiac signs, a hemorrhagic or serohemorrhagic pericardial effusion, cardiac dysfunction or failure in the presence of known malignant disease, postural change in murmurs, and localized fixation of a cardiac contour Aside from some of the intra atrial myxomas and the pedunculated benign fibromas, *there is probably little to be offered in the way of surgical relief*

TUMORS OF THE LUNG

By far the commonest tumor to affect the thorax is primary bronchogenic carcinoma which in numbers alone exceeds all of the other primary tumors combined Once considered to be a relatively rare condition partly because it was unrecognized and unappreciated, it now ranks as number two if not first, among all types of carcinomas For the purposes of description tumors of the lung may be considered under benign, malignant metastatic tumors, and inflammatory lesions

BENIGN TUMORS OF THE LUNG

Bronchial Adenoma
Fibroma (Benign Fibrous Mesothelioma)
Hamartoma (Chondroma)
Cyst Bronchial
Emphysematous
Myoma Leiomyoma
Rhabdomyoma
Arteriovenous Fistula

MALIGNANT PRIMARY TUMORS OF THE LUNG

Bronchogenic Carcinoma Squamous Cell Carcinoma
Adenocarcinoma
Small Cell Carcinoma
Large Cell Carcinoma
Bronchiolar Carcinoma (Alveolar Cell Carcinoma)
Primary Sarcoma
Superior Pulmonary Sulcus Tumor
Malignant Mesothelioma

SOLITARY METASTATIC TUMORS OF THE LUNG

Carcinoma of the Kidney
Soft Tissue Sarcoma
Carcinoma of the Colon
Carcinoma of the Ovary
Carcinoma of the Breast
Carcinoma of the Thyroid
Hodgkin s Disease

INFLAMMATORY LESIONS

Granuloma Tuberculosis
Histoplasmosis
Actinomycosis
Blastomycosis
Oil Pneumonitis
Pulmonary Abscess
Infected Cysts
Isolated Pulmonary Nodule

TUMORS OF THE TRACHEA

Squamous Cell Carcinoma
Cylindroma
Adenoma
Hemangioendothelioma
Benign Polypoid Tumor

BENIGN TUMORS

Bronchial Adenoma

Adenoma of the bronchus usually develops in one of the major bronchi producing its symptoms by bronchial obstruction or local bleeding but usually does not produce an x ray shadow by itself Occasionally, however the tumor may grow to considerable size producing the shadow of a local tumor mass or if more peripherally located presenting as a

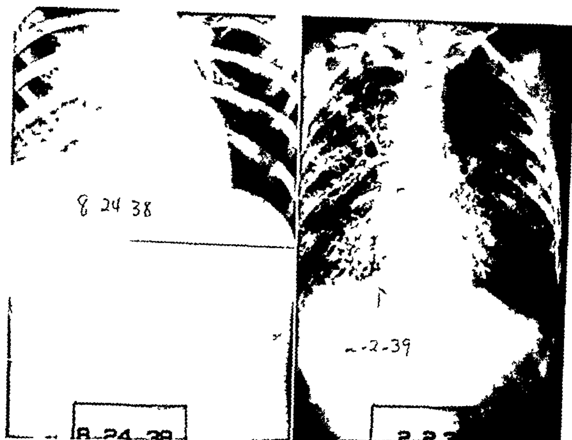


Plate 65 Bronchial Adenoma J W female age 8

Fig 1 Obstruction due to tumor
Fig 2 Filling defect in bronchus from tumor Secondary bronchiectasis

Rarely a huge tumor mass is produced The tumor may present as an intraluminal mass as *an intra and extrabronchial tumor or it may* be entirely extrabronchial Developing as it does in the larger bronchi approximately 90% of the tumors may be visualized bronchoscopically and biopsy material obtained These tumors are usually seen in a younger age group than bronchogenic carcinoma and somewhat more commonly in females than in males There are notable exceptions however with tumors occasionally being discovered in patients sixty or even seventy years of age

Growth is usually slow sometimes extending over a period of fifteen to twenty or thirty years Symptoms are produced by obstruction with cough wheezing dyspnea by infection distal to obstruction fever expectoration and by bleeding from local ulceration upon exertion with the menstrual period or from secondary bronchiectasis The possibility of such a tumor must be considered in any patient presenting bronchial obstruction and *suppuration or pulmonary bleeding* Careful bronchoscopic examination should be made with biopsy to confirm the diagnosis Some of these tumors are extremely vascular and very serious bleeding may be encountered following biopsy Before attempting such a biopsy the bronchoscopist should be adequately prepared to maintain a free airway and to control the bleeding

The bronchial adenoma commonly called benign from the microscopic picture may not be at all benign from the patient's standpoint as it can kill by hemorrhage pulmonary suppuration or sepsis and by septic metastasis to the brain or other sites Microscopically they are classified as benign and yet approximately ten per cent of them metastasize to regional lymph nodes liver and a few more extensively Histologically they may be either the carcinoid or the cylindromatous type with metas



Plate 66 Adenoma of Bronchus Mrs S age 56

Fig 1 Total atelectasis right lung
Fig 2 Specimen Adenoma of right main bronchus with bronchiectasis

tasis percentage wise being approximately three times as common in the cylindromatous type as in the carcinoid although the carcinoid type of tumor occurs almost three times as commonly as the cylindromatous type

From the standpoint of the local tumor alone endoscopic removal with any degree of completeness is possible only in the completely endobronchial tumor In tumors of the collar button or dumb bell type only the presenting intraluminal portion of the mass can be removed endoscopically This procedure may control bleeding and may relieve bronchial obstruction and infection and give complete symptomatic relief The regrowth of the tumor from the basal residual portion may be very slow with the bronchial mucosa growing over the defect leaving the patient free of symptoms for months or years Many patients so treated however are left with secondary pulmonary suppuration bronchiectasis and the symptoms therefrom in spite of removal of the local obstructing tumor

Direct surgical removal of the local tumor both extraluminal and intraluminal by bronchotomy and local resection may likewise remove the tumor but not relieve the local inflammatory residue Partial lobectomy and lobectomy or even pneumonectomy may be indicated and frequently is by the size and position of the tumor and by the extensive pulmonary suppuration distal to it Enlarged lymph nodes encountered at the time of surgical exploration may be the result of pulmonary suppuration or may be involved by direct extension or by metastasis from the original tumor site The possibility of metastasis must always be borne in mind and an adequate lymph node dissection carried out The prognosis in the early lymph node in

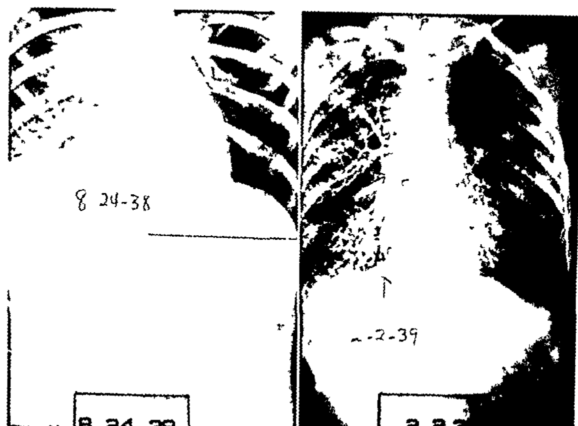


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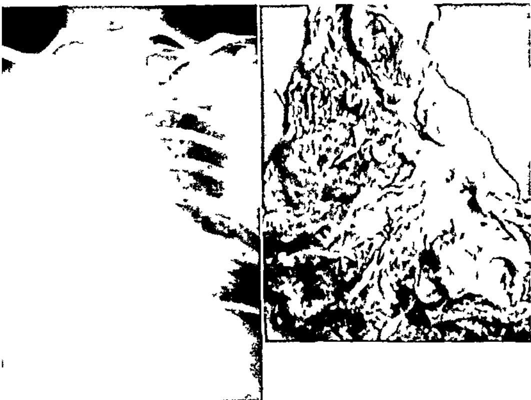


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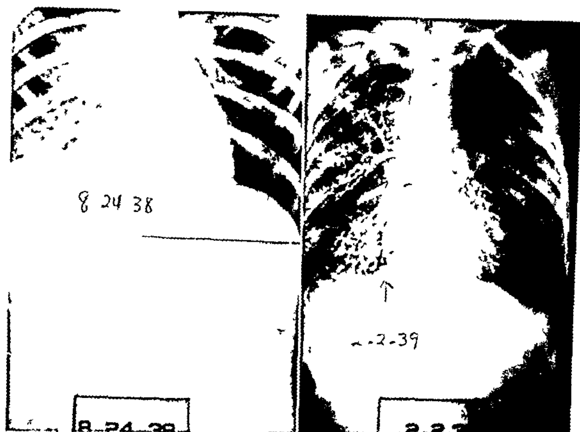


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Plate 67 Sequestration of Lung B W female age 15

Fig 1 and 2 Infiltration and cystic change right lower lobe
Fig 3 Specimen Cannula in abnormal artery from aorta entering at base of lobe
Fig 4 X ray—lipiodal injection of artery

vasion may still be excellent, but even when distant metastasis occurs, the patient may survive for a number of years

Hamartoma (Chondromatous Hamartoma)

Cartilagenous tumors of the lung commonly called chondroma, hamartoma or chondromatous hamartoma, are now being reported with increasing frequency following their discovery on routine hospital admission or survey films The majority do not produce symptoms as many lie well out in the substance of the lung Occasionally the tumor may lie close to a main bronchus or in its wall and cause bronchial obstruction and secondary suppuration The majority of tumors discovered are small, not more than 3 cm in diameter though some reach huge proportions They are ordinarily rather rounded and sharp-cut in appearance but may be somewhat lobulated or umbilicated on certain views Ordinarily uncalcified, they may show a characteristic cauliflower-like appearance if calcium deposits are present The mass may remain static and unchanged over a period of months or years, or it may show a surprising rate of growth, doubling or trebling in size over a period of a few months or years

When the lung is exposed in the operating room, the mass usually does not show on the surface though occasionally it does, but it is easily palpated as a firm, slightly irregular rather freely movable mass superficially located in the segment Those which lie deeper in the lung are usually more fixed and less readily accessible If the lung is incised over the presenting mass, the cartilagenous tumor may pop out like a peanut from its shell The white cartilagenous mass appearing like a small cauliflower is easily recognizable grossly Care must be exercised if tumors are removed in this way that some of the small surface projections are not displaced and allowed to remain in the lung as a possible nidus for regrowth of the mass, if experience with other cartilagenous tumors can be applied here A safer means of excision is by segmental or peripheral wedge excision We know of no reported cases of recurrence or malignant change in this type of tumor

Fibroma of the Lung (Benign Fibrous Pleural Mesothelioma)

Rarely a localized fibrous tissue tumor of the lung presents as an isolated pulmonary nodule Usually, however, a benign fibrous tissue tumor of the lung presents as a localized superficial tumor mass frequently pedunculated and attached to the lung by a small pedicle—the benign fibrous pleural mesothelioma The tumor is usually asymptomatic and discovered on routine films Some of these tumors produce digital and joint changes somewhat similar to hypertrophic pulmonary osteoarthropathy encountered with certain other tumors and with bronchogenic carcinoma They are usually not recognized preoperatively as such, but they should be suspected if joint pains and clubbing or swelling of the fingers is present associated with a peripheral tumor which may move freely on respiration

A diagnostic pneumothorax will certainly demonstrate the free mobility of the tumor and may demonstrate its pedicle These tumors vary in size from a few centimeters up to large tumors 10 to 15 cm in diameter They ordinarily arise from the peripheral surface of the lung with a pedicle no more than 1 cm in diameter containing the vascular supply Occasionally they arise from the parietal pleura or from pericardium or even the epicardium The tumor may appear to be very red and angry with local fibrin deposits on the surface but is usually not adherent to surrounding structures Although they are ordinarily benign clinically and microscopically, there is roughly a 15% chance of recurrence which would raise the question if at least some were not sarcomatous from the start

The base of the tumor including a fair segment of adjacent lung should be excised rather than merely clamping and ligating the pedicle itself Following excision of the tumor, there may be a dramatic disappearance of clubbing, joint swelling stiffness and pain within seventy-two hours The author has seen one instance of such dramatic disappearance of joint symptoms following removal of the first tumor with recurrence of the joint difficulties



Plate 67 Sequestration of Lung B W female age 15

Fig 1 and 2 Infiltration and cystic change right lower lobe

Fig. 3 Specimen *Canula in abnormal artery from aorta entering at base of lobe*

Fig 4 X ray—Lipiodal injection of artery



Plate 68 Congenital Pulmonary Cyst—Infected H S female age 22 months

11 years later antedating the discovery of a recurrent tumor by several months Again there was prompt subsidance of the joint symptoms within 3 days following the removal of the recurrent tumor which was a low grade sarcoma

Pulmonary Cyst

A true pulmonary cyst may occur at any age even in the newborn If fluid filled it may present as a smooth rounded shadow in the lung field and either remain static or slowly increase in size producing symptoms by pressure only It may discharge its contents suddenly into the lung through a bronchial opening asphyxiating the patient or more slowly permitting the patient to expectorate the fluid Secondary infection of residual cyst wall may or may not occur The cyst may persist as an air filled pneumatocele with no symptoms for a long period of time Pulmonary hemorrhage or bleeding into the cyst may occur months or years later Occasionally a carcinoma may develop in the cyst wall

A cyst may occasionally be shelled out of the parenchyma of the lung preserving most of the lung substance Others may require a segmental excision or partial lobectomy or even a lobectomy for complete removal An air containing pulmonary cyst may have a check valve mechanism in the communicating bronchus producing a ballooning cyst with pressure symptoms These cysts as well as the fluid filled cysts may show bronchial epithelium and bronchial wall elements in various areas Most of these cysts are unilocular though occasionally they are multilocular



Plate 69 Pulmonary Cyst Bronchogenic Carcinoma D N male age 48

Fig 1 and 2 Cyst right lower lobe on bronchogram Bronchoscopy revealed no tumor Carcinoma in pulmonary cyst with mediastinal metastases

Either type may be seen in the newborn infant If distention gives respiratory difficulty excision may be required even in very small infants to relieve the pressure symptoms

The most commonly encountered cystic changes in the lung are *bullous emphysema* emphysematous blebs or the vanishing lung none of which are likely to be confused with other thoracic tumors They may be seen even in the newborn or children of small size but unless they are causing serious respiratory embarrassment should not be treated surgically until the child is older and the surgery can be carried on with less risk Parasitic cysts and cysts following infection will be considered under inflammatory lesions

Arteriovenous Fistulae (Arterial Aneurysms)

The clinical picture of well developed arteriovenous fistulae of the lung with cyanosis clubbing of the fingers and toes polycythemia and perhaps a localized bruit or thrill over certain areas of the lung without cardiac enlargement is quite generally recognized As sociated with this may be an x ray shadow suggestive of *tumor with a vascular shadow lead*ing to it as demonstrated on special x ray films or planigrams The x ray shadow may be a rounded tumor mass but is quite likely to be somewhat irregular The fistulae may be single or multiple unilateral or bilateral There may be an associated history of familial telangiectasis or the demonstration of cutaneous or mucous membrane telangiectases in the patient (the Osler Weber Rendu syndrome) Cyanosis polycythemia and clubbing may have been present before puberty but not infrequently develop thereafter The condition may not be difficult to diagnose if one is familiar with it Changes in the size of the

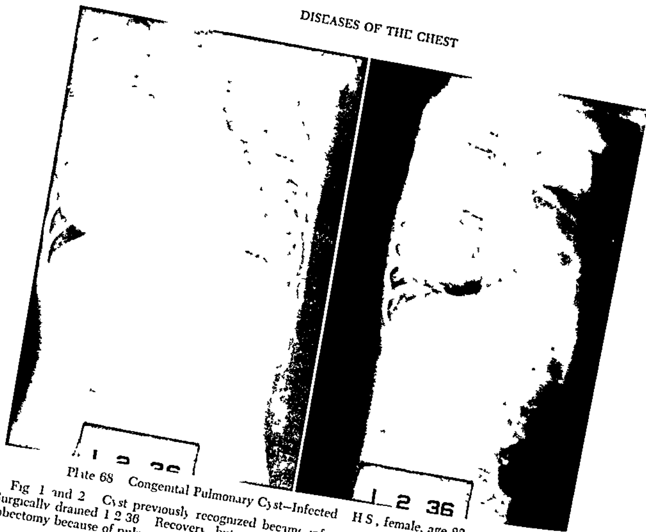


Plate 68 Congenital Pulmonary Cyst—Infected

Fig 1 and 2 Cyst previously recognized became infected following attack of follicular tonsillitis H S, female, age 22 months Surgically drained 1 2 36 Recovery, but air filled cyst remained Eighteen years later, right lower lobectomy because of pulmonary hemorrhage and bleeding into cyst

11 years later, antedating the discovery of a recurrent tumor by several months Again there was prompt subsidance of the joint symptoms within 3 days following the removal of the recurrent tumor which was a low grade sarcoma

Pulmonary Cyst

A true pulmonary cyst may occur at any age, even in the newborn If fluid-filled, it may present as a smooth rounded shadow in the lung field, and either remain static or slowly increase in size, producing symptoms by pressure only It may discharge its contents suddenly into the lung through a bronchial opening, asphyxiating the patient or more slowly, permitting the patient to expectorate the fluid Secondary infection of residual cyst wall may or may not occur The cyst may persist as an air filled pneumatocele with no symptoms for a long period of time Pulmonary hemorrhage or bleeding into the cyst may occur months or years later Occasionally a carcinoma may develop in the cyst wall

A cyst may occasionally be shelled out of the parenchyma of the lung, preserving most of the lung substance Others may require a segmental excision or partial lobectomy or even a lobectomy for complete removal An air containing pulmonary cyst may have a check valve mechanism in the communicating bronchus producing a ballooning cyst with pressure symptoms These cysts as well as the fluid filled cysts may show bronchial epithelium and bronchial wall elements in various areas Most of these cysts are unilocular though occasionally they are multilocular

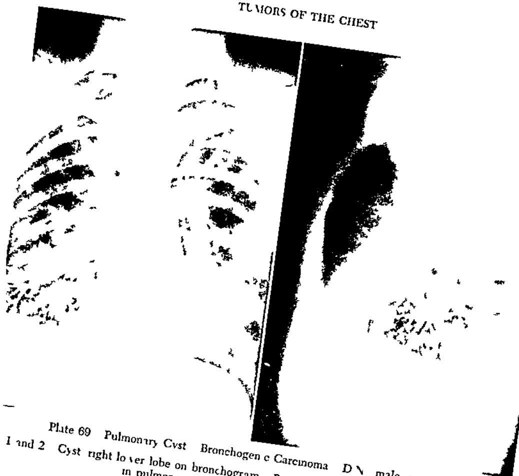


Plate 69 Pulmonary Cyst Bronchogenic Carcinoma D N male age 48
Fig 1 and 2 Cyst right lower lobe on bronchogram Bronchoscopy revealed no tumor Carcinoma in pulmonary cyst with mediastinal metastases

Either type may be seen in the newborn infant If distention gives respiratory difficulty excision may be required even in very small infants to relieve the pressure symptoms

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Plate 70 Fibrous Mesothelioma—Sarcoma A C female

Fig 1 1941 age 53 Benign (?) fibrous tumor removed Had joint changes which disappeared in few days

Fig 2 1953 age 65 Rheumatism 6 months Another tumor same site found and removed Joint changes cleared in 72 hours Tumor reported as fibrosarcoma—low grade

Fig 3 1956 age 68 Another tumor discovered on routine x ray No joint changes Tumor removed from lung Fibrosarcoma low grade



Plate 71 Benign Fibrous Mesothelioma L McF female age 46

Fig 1 Tumor left base

Fig 2 Detail Benign fibrous mesothelioma pedunculated left base No joint symptoms

mass on the Valsalva or Muller maneuvers are diagnostic

Cardiac catheterization or angiocardiography will easily confirm the diagnosis The amount of cyanosis or arterial oxygen desaturation varies with the size of the tumor and the amount of the shunt Some of these lesions may remain static for long periods of time and cause no symptoms If there is increase in size the amount of shunt increases with increasing oxygen desaturation Additional areas may appear as small lesions previously unrecognized develop in the same or contralateral lung Pulmonary hemorrhage slight to serious and even fatal may occur Brain abscesses have been reported

Surgical extirpation of the involved area by segmental resection single or multiple or more extensive resection is the procedure of choice if lesions are limited and localized and is curative if no other lesions remain Careful studies must be made, however, before extensive surgery is carried out because of the possibilities of bilateral involvement Some of the lesions are easily recognizable in the operative field by the surface appearance and by the presence of a localized bruit or thrill while others in deeper locations may be found only with difficulty hence the advisability of accurate localization before surgery is attempted Following the removal of all shunts polycythemia cyanosis and oxygen desaturation should disappear Failure to do so would indicate residual unrecognized lesions

Rare Benign Tumors

There are scattered reports in the literature of very rare benign localized tumor masses such as lipomas fibromas neurofibromas leiomyomas rhabdomyomas none of which

apparently can be diagnosed preoperatively but only by microscopic examination after excision They present as rounded smooth rather sharp cut shadows on x ray film with nothing to differentiate them from the isolated pulmonary nodules

Isolated Pulmonary Nodules (Coin Lesions)

Since extensive x ray surveys of apparently normal people have been carried out and since many hospitals have instituted a program of routine admission chest x rays of all patients physicians have been confronted with the problem of the isolated pulmonary nodule frequently miscalled the "coin lesion about which nothing was previously known The single chest film may prove deceptive as pigmented moles sebaceous cysts or a large nipple may cast a shadow easily confused with that of an intrapulmonary nodule Simple inspection or palpation and the lateral chest film will easily demonstrate these The nodules are found in the parenchyma of the lung on either side and at any level from top to bottom If the term is restricted to shadows which are 3 cm or less in size as we feel it should be this automatically eliminates a number of carcinomatous masses both primary and metastatic which have unnecessarily loaded some reported series on the malignant side

Much time and effort a great deal of thought and much more money has been expended by many investigators attempting to determine the nature of these lesions preoperatively hoping thereby to be able to decide which nodules may and which may not be safely allowed to remain within the chest These lesions are almost invariably asymptomatic They may be caused by a wide variety of pathological conditions benign malignant metastatic or inflammatory in origin These include benign tumors such as fibromas neurofibromas lipomas leiomyomas rhabdomyomas chondromas or hamartomas pulmonary cysts arteriovenous fistulae bronchial adenomas primary malignant nodules of primary bronchogenic carcinoma and sarcoma the apparently solitary metastases from hypernephroma, soft tissue sarcoma carcinoma of the thyroid colon ovary and breast and the inflammatory lesions of tuberculosis histoplasmosis brucellosis, coccidiomycosis and oil pneumonitis

Many attempts have been made to diagnose specific lesions or differentiate between one and another in this large group but as yet no definite accurate criteria have been found to diagnose any of the lesions with certainty A positive tuberculin histoplasmin or coccidioidin test does not indicate that the lesion in question is of that etiology The presence of calcium while suggestive of a benign lesion does not with certainty establish such a diagnosis for malignancy may develop in an area of previous calcification or calcification may develop in a degenerating portion of a tumor The presence of umbilication or notching on one margin of the shadow does not prove malignancy though it may occur in this group but it has also been seen repeatedly in inflammatory nodules and hamartomas Comparison of a recent x ray film with previous films may help greatly because if the nodule has been present and has remained unchanged for a matter of 5 to 10 years the percentage chance of its being malignant is greatly reduced This does not completely eliminate the chance of malignancy for occasional nodules of from 5 to 7 or 8 years duration have been shown to be malignant in nature

The common practice of watching the lesion on serial x rays for growth or nongrowth leaves the clinician in a sort of fool's paradise The fact that the lesion does not grow in 6 months or a year does not rule out malignancy yet it certainly wastes valuable time Increase in size of the nodule will usually stampede every one concerned into hurried action yet while it may it frequently does not indicate a malignant lesion for growth has been observed in granulomas of both tuberculous and histoplasmosis etiology in abscesses and cysts and even in chondromatous hamartomas The presence of calcium within the nodule may not be seen on ordinary chest films but can be demonstrated with greater certainty by a planigraphic series Calcium deposits in concentric rings or in a cauliflower like pattern may well suggest that the lesion is a granuloma of histoplasmosis or tuberculosis or a chondromatous hamartoma

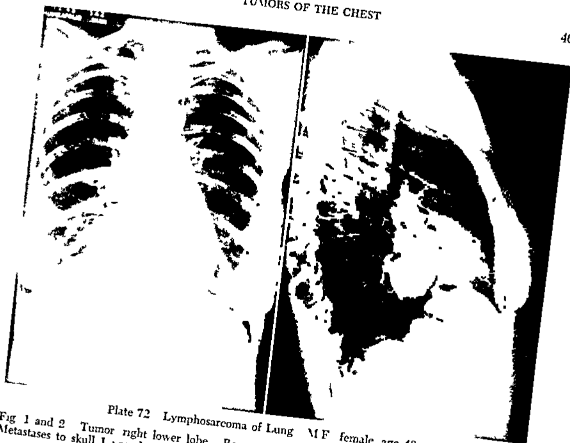


Plate 72 Lymphosarcoma of Lung M F female age 48
Fig 1 and 2 Tumor right lower lobe Resected 1950 lobectomy Mediastinal nodes negative Metastases to skull 1 year later Treated by x ray and disappeared No recurrence 5 years later

The age of the patient has a distinct bearing on the possibilities of malignancy in an isolated nodule If the patient is under the age of thirty few malignant nodules will be encountered except for an occasional one of metastatic origin Beyond the age of 40 the problem becomes altogether different especially in males for the percentage of malignancy increases rapidly and exceeds 60% in the upper age group Over a large series however approximately 40% have been reported as malignant 40% as inflammatory and 20% as benign cysts or tumors Even among the so called benign lesions there are some which may not be innocent from the patient's standpoint for a tuberculous granuloma or caseous abscess may drain into the bronchus and disseminate tuberculosis A bronchial adenoma may grow obstruct a bronchus and lead to suppurative disease of the lung and a few of them metastasize Pulmonary cysts may bleed or become infected with abscess formation

Considering the whole subject in patients under the age of thirty one may with a fair degree of safety adopt a temporizing policy of doing nothing but following the lesion In patients over this age however unless there is some contraindicating factor the only safe policy is to remove the offending lesion for immediate pathological examination while the chest is still open so that the surgeon may carry out additional surgery without further delay if necessary The risk of thoracotomy with local excision of an isolated pulmonary nodule is very small a fraction of 1% The period of hospitalization is short and the relief to the patient from establishment of a definite diagnosis is well worth the expense and the effort Theoretically at least this program should afford opportunity for early treatment of a number of malignant lesions perhaps with

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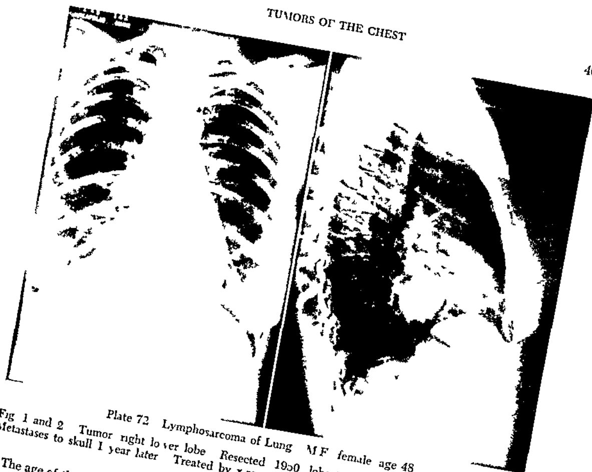


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Plate 73 Metastatic Carcinoma from Colon S F male age 74

Fig 1 Metastatic tumor and abscess present 2 years before patient would consent to operation Right middle lobectomy Patient survived 2 years following resection dying from metastases

a better prognosis From the practical stand point however this has not always been true

Sequestration of the Lung

Sequestration of the lung is a rare congenital anomaly in which a portion of the lower lobe *either right or left usually basal segments* only becomes physiologically cut off from the rest of the lung and receives an arterial supply direct from the aorta or *a division of the* celiac axis entering through the base of the inferior pulmonary ligament The venous return of the blood supplied by the *anomalous* artery is through the inferior pulmonary vein Clinically the lesion may present as a triangular shadow at the base not infrequently associated with cystic changes within it The patient may *present no symptoms* The clinical picture is often very confusing with the possibility that the condition is produced by a carcinoma usually justifying exploration Cystic changes are usually demonstrable The author has removed one such lobe in which cystic change was present but there was also a carcinoma adjacent to it These patients do not present cyanosis clubbing polycythemia as the patients with arteriovenous fistulae do and do not show cardiac enlargement for the blood goes through a capillary bed in the sequestered segment before entering the pulmonary vein Surgical excision is the treatment of choice The surgeon must ever be aware *of the possi* bility of this anomaly when resecting a lower lobe particularly in mobilizing the inferior *pulmonary ligament of an adherent lower lobe* as serious bleeding may be encountered if the incoming artery sometimes a centimeter in diameter is injured

SOLITARY METASTATIC TUMORS OF THE LUNGS

Metastatic tumors in the lung are more commonly multiple rather than single Occasionally an apparently solitary or even truely solitary metastatic lesion may be encountered Such solitary metastases have been reported from hypernephroma sarcoma (soft tissue or bone) and cancer of the thyroid colon ovary and occasionally from the breast If there is a history of such previous tumor the suspicion of a metastatic lesion should immediately arise If on the other hand the original tumor is yet silent the metastatic nature of the condition may not even be suspected Even more confusing may be the situation in which the metastasis involves a bronchus in which case the clinical picture may be identical with that produced by an obstructing primary bronchogenic carcinoma If the presenting tumor mass in the bronchus is accessible for biopsy the situation may be readily cleared by microscopic examination of the biopsy specimen Such bronchial obstructive lesions identified by bronchoscopic biopsy have been found sec*ondary to hypernephroma* carcinoma of the colon and rectum seminoma of the testicle



Plate 74 Primary Bronchogenic Carcinoma Adenocarcinoma Mrs F age 57

Fig 1 1940 Isolated pulmonary nodule
Fig 2 11-5-47 Progression of tumor resectable not curable

carcinoma of the breast and in Hodgkins disease

The surgical removal of a known metastatic lesion may at times be well worth while, especially in some of the slower growing tumors such as hypernephroma carcinoma of the colon and less frequently of the breast thyroid Wilms tumor of the kidney or a low grade sarcoma In general it is probably advisable to wait for a time following the discovery of the tumor before removing it if a metastatic lesion is suspected in order to gain a little more certainty that the lesion is solitary which all too frequently is not the case While occasional very gratifying results are obtained the overall salvage rate is not too high

INFLAMMATORY LESIONS

There are a number of inflammatory lesions which may be confused with chest tumors The granulomas of tuberculosis, histoplasmosis, and coccidiomycosis have already been mentioned under isolated pulmonary nodules Other inflammatory conditions such as pulmonary abscesses infected pulmonary cysts blood filled pulmonary cysts and echinococcus cysts may produce shadows which simulate a localized tumor within the lung Oil pneumonitis pulmonary tuberculosis and pulmonary actinomycosis or blastomycosis may present infiltrations in the lung which may exactly simulate the picture produced by bronchiogenic carcinoma

Probably more errors are made in the opposite direction treating a malignant lesion as an inflammatory one rather than treating an inflammatory lesion as a malignant one In fact one clinician has aptly remarked that he has yet to see a carcinoma of the lung cured by treatment with penicillin or other antibiotics

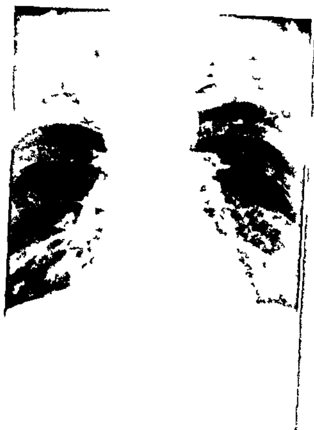




Plate 75 Primary Bronchogenic Carcinoma Squamous J K male age 61

Fig 1 Apical segment obstructed
Fig 2 Bronchogram—apical segmental bronchus blocked
Fig 3 Specimen Carcinoma of apical segmental bronchus without lymph node involvement Patient died of pulmonary embolism seventh day ambulating since second day



Plate 76 *Primary Bronchogenic Carcinoma Squamous* F S *male* age 63

Fig 1 and 2 Obstruction *right basal* segments Right *pneumonectomy lymph nodes involved* 11 6 50 *Patient remains in* good health 1956

Whenever the clinician is tempted to make a diagnosis of virus pneumonia or unresolved pneumonia he should immediately stop and take stock remembering that he has a diagnostic problem on his hands and that neither of these is a good diagnosis unless all other possibilities have been ruled out for once a diagnosis has been made that condition is treated whether it be the correct one or not The differential diagnosis may not be an easy one though there are often many things in the history mode of onset mode of progression and response which may give a clue to the correct one A history of dysphagia or a spell of unconsciousness alcoholic or otherwise may give the clue to an aspiration pneumonitis or abscess A history of exposure to silica asbestos or other industrial hazards may suggest a pneumoconiosis or silicosis A few neurological findings may base the aspiration on a neurogenic basis A history of strangling may be the clue to a retained foreign body in the lung The history of repeated ingestion of mineral oil or repeated or constant use of an oil atomizer or nose drops may be the clue to an oil pneumonitis An alcoholic history may suggest an aspiration pneumonitis or a Friedlander s pneumonia as may the presence of marked gingivitis pyorrhea or a poor gag reflex

The character of the sputum may suggest a lung abscess though it is well to remember that such occur not infrequently in and distal to a bronchogenic carcinoma Study of the sputum for predominant organisms or tubercle bacilli and later culture for secondary organisms and their sensitivity are of vital importance One must not however routinely wait for tuberculosis cultures and thus waste an additional two months before making a diag

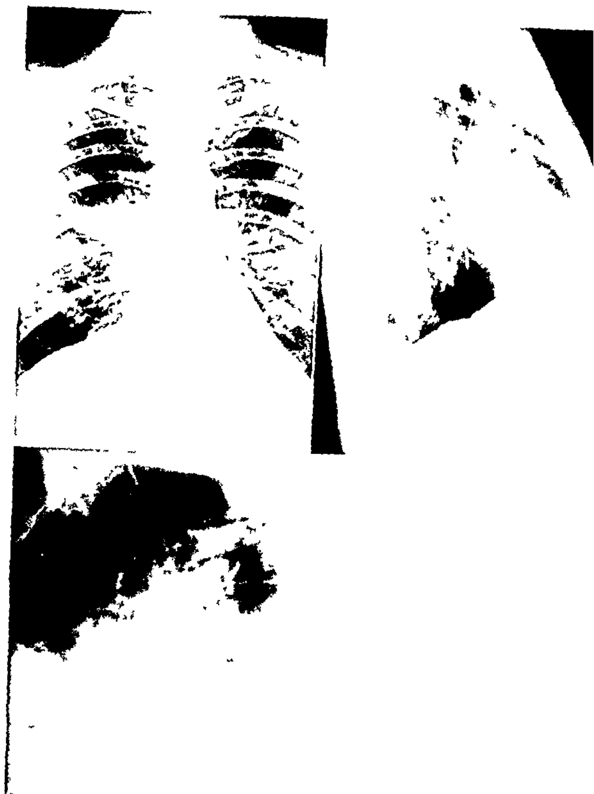


Plate 77 Primary Bronchogenic Carcinoma Squamous Cell J V McC male age 58

Fig 1 and 2 Tumor obstructing anterior segment of upper lobe
Fig 3 Bronchogram—rat tail obstruction of anterior segment bronchus Right pneumonectomy
Patient survived 7 years, dying from coronary heart disease.



Plate 78 Primary Bronchogenic Carcinoma Squamous Cell F R male age 72

Fig 1 and 2 Carcinoma right lower lobe s hcosis grade I R ght lower lobectomy 5 13-48 Patient is living and well at age 81

nosis of carcinoma Such diagnostic problems require extensive and complete study History physical examination x ray studies from various views planigraphic study and bronchoscopy and bronchography cell studies of sputum bronchial aspirate and biopsy of suspicious areas in the bronchial tree all have their place in reaching the correct diagnosis though all do not have to be done in each particular case Clinical judgement and discrimination may save the patient time and money in arriving at the correct answer Chest wall pain is encountered in tumor though it may occur in tuberculosis and especially so in actinomycosis and blastomycosis The development of draining sinuses in the chest wall should always call attention to the possibility of tuberculosis actinomycos s or blastomycosis Surgical drainage or excision may be available for a number of these inflammatory lesions

PHANTOM TUMOR

Occasionally one is confronted with a patient whose x rays show a smooth rounded shadow 4 to 5 cm in diameter usually in the lower half of the chest simulating an intrapulmonary tumor Subsequent fluoroscopic examination or additional set of x ray films may f ul to show any evidence of tumor the shadow having disappeared in a matter of two or three weeks These phantom tumors usually are caused by a localized fissure accumulation of fluid which either absorbs in a short period of time or shifts its position to destroy the contour suggesting tumor Another similar situation is encountered in patients who have had a previous pneumothorax or pleural effusion in whom a condensation of coagulated fibrin (a pleural mouse) persists as a localized mass against the chest wall or in the costophrenic angle suggesting a localized tumor mass If







Plate 79 Primary Bronchogenic Carcinoma Squamous Poorly Differentiated R W male age 38

Fig 1 and 2 Large tumor

Fig 3 Specimen Pulmonary osteoarthropathy first symptom of lung lesion Could not close hands or milk cows Right pneumonectomy Pain and swelling of hands disappeared within 62 hours Patient died from cerebral metastases 6 months later

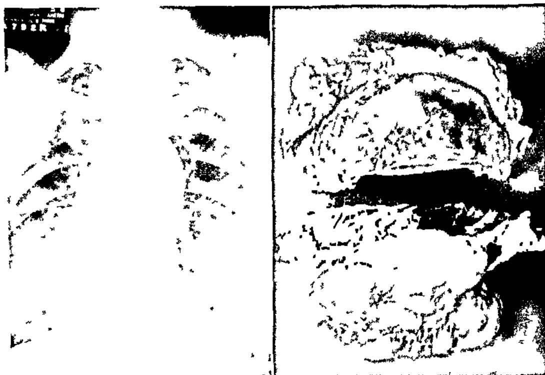


Plate 80 Primary Bronchogenic Carcinoma Squamous Poorly Differentiated B C male age 70

Fig 1 Peripheral mass

Fig 2 Tumor and segment of chest wall Direct tumor invasion of chest wall by peripheral carcinoma Patient died 3¹/ months later with extensive metastases

it is recognized as such nothing need be done about it as they do no harm

PULMONARY CYSTS

Pulmonary cysts congenital acquired or of bullous emphysematous origin if air filled cause no confusion with other tumors of the chest If fluid filled from infection hemorrhage or secretion from the cyst wall the rounded contour and smooth margins readily give the clue to the nature of the condition Local excision of the cyst preserving as much pulmonary tissue as possible is the procedure of choice

TUMORS OF THE TRACHEA

Tumors of the trachea are very rare in comparison to other tumors of the chest especially in relation to bronchogenic carcinoma The possibility of such a condition is usually not even considered in the patient complaining of cough and wheezing and x ray films usually give no indication of its presence Any patient in the carcinoma age group with a recent history of cough and wheezing is not to be passed up as an asthmatic but should be investigated to determine the cause of his wheezing The bronchoscopist may overlook a lesion of the tracheal wall in his hurry to get from the vocal cords down to the carina looking for a cause for the wheeze A coating of iodized oil on the tracheal wall will give best delineation of the site of the tumor and its extent The exact nature of the tumor mass can only be determined by direct biopsy of the lesion

The commonest types of tumors encountered are squamous cell carcinoma and cylindroma

and less commonly adenocarcinoma and hemangioendothelioma. The slow growing late metastasizing cylindroma offers the best chance for surgical treatment. In the carcinomas the squamous cell carcinoma may offer a slightly better chance than the adenocarcinoma type.

Primary treatment in these patients consists of freeing the airway if it is seriously obstructed by the endoscopic removal of enough of the projecting mass to permit free breathing. Subsequently if the condition be localized and favorably situated with no evidence of local invasion or distant metastasis the possibilities of surgical removal may be considered. Local excision of the tumor from the tracheal wall preserving part of the trachea if possible with reconstruction of the wall by a *dermal or fascial patch* has been reported. If the entire circumference of the trachea has to be resected and the resulting defect is not too great end to end anastomosis may be feasible, otherwise a *polythene or other plastic splint* must be used. Tracheotomy must be done because these patients have a great deal of difficulty in clearing their secretions and require repeated aspirations. In the event that the tumor is not locally removable repeated clearing of the tracheal lumen endoscopically with local coagulation of the base may keep the trachea free enough for aspiration until other complications end the picture.

PRIMARY MALIGNANT TUMORS OF THE LUNG

Primary bronchogenic carcinoma is by far the commonest tumor of the chest; in fact in numbers it probably exceeds that of all other tumors combined. Primary bronchogenic carcinoma, bronchiolar carcinoma (alveolar cell carcinoma), primary pulmonary sarcoma, malignant mesothelioma and superior pulmonary sulcus tumors comprise the group of primary malignant tumors of the lung.

PRIMARY BRONCHOGENIC CARCINOMA

Primary bronchogenic carcinoma once considered to be a rather rare condition is now one of the most *frequent if not the most frequent* type of carcinoma in men. Although it may occur in any age group it is usually found in individuals beyond the age of 35 or 40 and is significantly more frequent in males than in females. It is perhaps *the greatest mimic* in the whole category of medicine. It can simulate the picture of almost any disease which affects the lungs and may be associated or coexistent with several of them. There is no magic formula for its recognition. *It is only* the clinician with a high index of suspicion for carcinoma who keeps the spectre of its possible existence always before him who will clinica[lly] recognize it in all its protean man[ifestations].

Primary bronchogenic carcinoma [...]us presents itself clinically in one of four ways or combinations thereof: (1) by producing bronchial obstruction, (2) by tumor mass, (3) by local extension or invasion, (4) by distant metastasis. It metastasizes by either lymphatic or vascular route and earlier and more widely than almost any other tumor. Metastases occur most frequently in the regional nodes, then widely, especially into the liver, mediastinum and to distant points involving almost any tissue in the body including the brain, thyroid, kidneys, adrenals, pancreas and even the skin. Metastasis may occur even before the lung tumor is demonstrable, especially brain metastasis which may simulate a primary tumor until the *microscopic examination* reveals the true nature of the condition.

Primary bronchogenic carcinoma developing in one of the major bronchi as it usually does sets up an irritation with cough and *perhaps a little sputum*, occasionally blood streaked, a little wheeze or squeak as the bronchial lumen is narrowed, following which the distal portion of the lung may show the trapped air sign of obstructive emphysema. Subsequently with more obstruction and atelectasis some tightness in the chest and perhaps some shortness of breath may be [...]ced. If infection develops in the ob[stru]cted area a pneumonitis simulating a clini[cal p]neumonia may occur. This often im

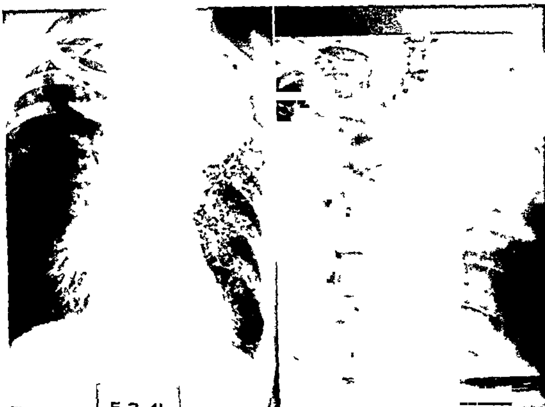


Plate 81 Primary Bronchogenic Carcinoma J G male age 62

Fig 1 Large tumor
Fig 2 Rib destruction by tumor

proves following chemotherapy to further confuse the picture If it does not clear in due time it may progress to a pulmonary abscess if the obstruction persists and secretions are not released Pleuritic pain pleural effusion or an empyema may follow

Spread of the tumor from the local site may occur locally in one of three ways through the blood stream through the lymphatics to adjacent bronchial or hilar lymph nodes and subsequently on to mediastinal lymph nodes or through the submucosal lymphatics proximally toward the larger bronchi or trachea to give rigidity to the bronchus and extension of the tumor at times for a considerable distance proximal to the presenting mass This narrowing and rigidity of the bronchial lumen may interfere with its normal respiratory activity and with aeration and drainage of the lung thus producing additional dyspnea and sepsis Enlargement of the lymph nodes along the bronchus or in the hilar region either from inflammatory reaction or tumor growth may likewise produce more narrowing and rigidity of the bronchus

As the process progresses proximally the subcarinal group of nodes may become involved widening the angle between the two bronchi at the carina and producing rigidity in that region As the paratracheal nodes become involved the increasing mass may constrict the trachea producing stridor or it may compress the esophagus adding dysphagia to the picture On the left side tumor may infiltrate or enlargement of the lymph nodes which lie posterior to and above the bronchus under the aortic arch may press upon or stretch the recurrent nerve producing a husky voice from left vocal cord paralysis Tumor tissue may progress outside of the lymphatics by direct

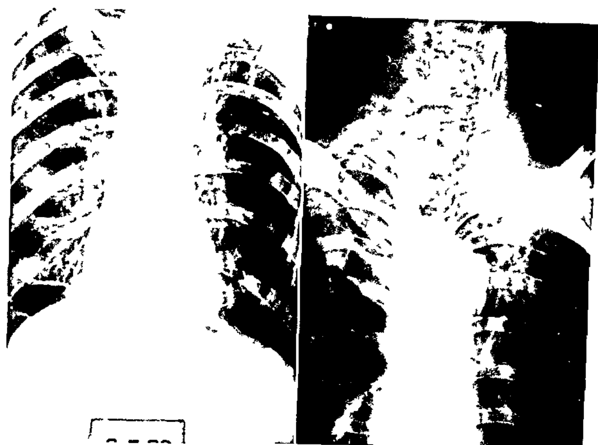


Plate 82 Superior Pulmonary Sulcus Tumor H T C male age 53

Fig 1 High apical tumor left—Pancoast syndrome
Fig 2 Rib destruction left apex

contiguity to involve the mediastinal pleura pericardium and later perhaps the phrenic nerve giving hemidiaphragmatic paralysis Such invasion not infrequently follows the anterior vein into the mediastinum with infiltration of the vein wall causing partial obstruction or even tumor growth within the lumen of the vein itself

Direct growth of tumor in the main bronchus may invade the esophagus causing partial obstruction and occasionally perforation and a bronchoesophageal fistula As mediastinal lymph node invasion progresses upwards more nodes become involved until one may find palpable carcinomatous nodes in the cervical region For a considerable time before these are evident grossly the involvement of the upper lymphatics may be demonstrated by removal of the lymph nodes overlying the scalenus anterior muscles and in the upper mediastinum by excision of the fat pad overlying the muscle and in the upper anterior mediastinum (scalenus anterior fat pad biopsy) Increasing size of the mediastinal lymph nodes may not only compress the trachea and esophagus causing stridor and dysphagia but also the superior vena cava interfering with the return of blood from the upper half of the body producing the superior vena caval syndrome Much more rarely the thoracic duct and the colaterals become obstructed with a resultant chylothorax or chylous ascites more commonly seen however in obstruction from lymphoblastoma than from carcinoma

Primary bronchogenic carcinoma may be accidentally discovered on x ray films as a small tumor mass peripherally though occasionally centrally located The mass frequently produces no symptoms until it attains considerable size with pressure and displacement of adjacent structures and peripheral involvement of the visceral pleura producing



Plate 83 Primary Bronchogenic Carcinoma G W male age 62

Fig 1 and 2 Pulmonary abscess secondary to carcinoma

pain fluid or chest wall invasion Proximal lymphatic spread occurs from this tumor as well as from those originating in the larger bronchi These tumors are bronchogenic carcinoma but apparently have developed from a smaller bronchus and occur less frequently than those in the major bronchi

Direct extension of the tumor to the visceral pleura may produce a pleural effusion often clear and serous but not infrequently bloody in which malignant tumor cells may be demonstrated by the experienced pathologist Although malignant tumor cells may be demonstrated in a bloody fluid from secondary metastatic lesions the presence of such an effusion containing malignant cells in the absence of a demonstrable tumor mass strongly suggests a primary bronchogenic tumor The presence of blood in fluid obtained at a primary tap is quite significant but that on secondary or subsequent taps less so because of the possibility of traumatic bleeding Extensive diffuse involvement of the visceral and parietal pleura may follow such implantation into the pleural cavity Occasionally large masses of tumor tissue occur simulating malignant mesothelioma of the pleura previously often diagnosed as endothelioma of the pleura before the significance of the primary lesion in the lung was recognized The growth of the tumor to the surface of the lung may not produce a pleural effusion but rather continue peripherally invading the chest wall destroying rib and causing chest pain and perhaps secondary invasion of the axillary lymphatics Chest wall symptoms may be the first clue to the underlying malignancy The Pancoast s syndrome is a common example of this direct chest wall invasion

Distant metastasis from primary bronchogenic carcinoma occur very commonly They may involve any tissue in the body including

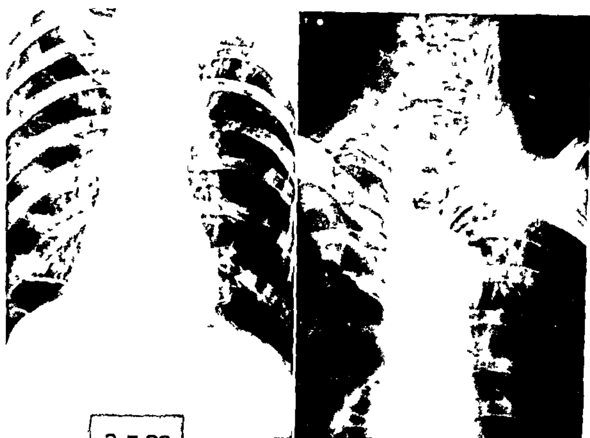


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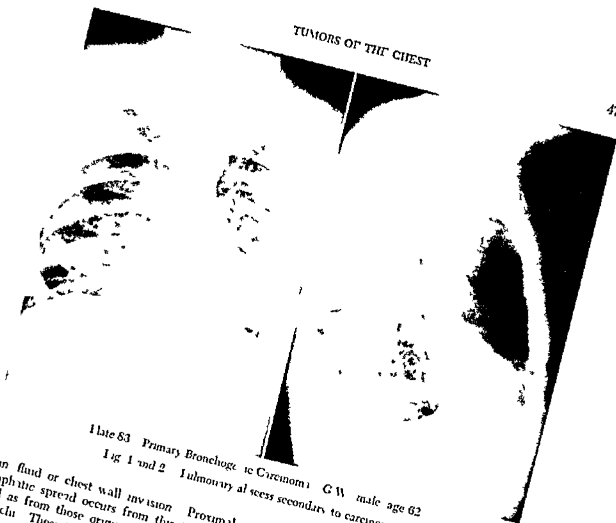


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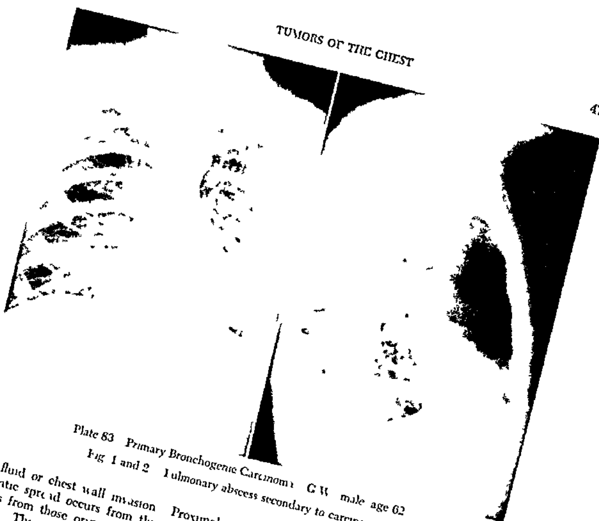


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Plate 84 Bronchiolar Carcinoma (Alveolar Cell Carcinoma) I C male age 48

Fig 1 11 12 44 Bilateral nodular tumor masses had been treated for 1 year for tuberculosis

Fig 2 7 19 45 Progression of tumors Progressive dyspnea Patient died a few months later

a number of the rare metastatic sites such as thyroid adrenals kidney pancreas brain and even skin Neurological surgeons have for years been cautious of exploring brain tumors apparently primary until they were satisfied that the chest x ray showed no evidence of tumor in the lung For years the massive liver involvement sometimes seen with late bronchogenic carcinoma confused pathologists and led them to search for an abdominal primary before the significance of the small pulmonary tumor was realized The significance of skin metastasis likewise was not appreciated for a long time

Microscopically primary bronchogenic carcinoma may be divided into four general groups squamous cell carcinoma large cell carcinoma adenocarcinoma and small cell carcinoma as reported by the Mayo Clinic group which made the most extensive and complete study of the relationships between cell type age distribution sex operability and prognosis Squamous cell carcinoma constituted 373 of the 1 400 cases studied (37 8%) It occurred rarely under the age of 40 and was predominantly a disease of males (23 59% occurred in females) It occurred predominantly in the larger bronchi with bronchoscopic biopsy positive in 64 5% Cytologic studies were positive in 72% Seventy one per cent of the patients were explored and 71% of this group were resected There was a 50% 2 to 5 year survival in this group

Large cell carcinoma constituted 40 2% of the group with 14 6% found in females The relationship of central to peripheral location of the tumor was 1 4 to 1 whereas in squamous cell carcinoma it was 1 9 to 1 for small cell carcinoma 27 7 to 1 for adenocarcinoma 0 54 to 1 Bronchoscopic biopsy was positive in

41.3%. Cytologic studies were positive in 90%. 55% of the patients who survived resection were dead within 2 years. Prognosis for this type of tumor is considerably poorer than for squamous cell carcinoma.

Adenocarcinoma constituted 13.2% of the whole series. There were many more of these tumors in a peripheral location than any of the other types. Bronchoscopic biopsy was positive in only 25% of the patients. Cytology was positive in 80%. 18.7% of the group occurred in females; two-thirds of the patients who survived resection were dead within 2 years.

Small cell carcinoma constitutes but 8.8% of the whole series. The majority of the tumors occurred in the fifth, sixth and seventh decade with the predominance of male patients over female patients 29 to 1. Bronchoscopic biopsy was positive in 76% and cytologic study positive in 93%. Only 2 of the 15 patients operated upon survived more than $2^{1}/_{4}$ years.

Which patients should be suspected of harboring bronchogenic carcinoma? The more conscious the clinician becomes of the prevalence of primary bronchogenic carcinoma, the more patients will be found to harbor that condition. If the physician will always remember that all patients who wheeze are not asthmatic, there will frequently be less delay in the diagnosis of a bronchial obstructive lesion. We feel that the following patients should be studied carefully for suspicion of harboring a bronchogenic carcinoma: patients who present a wheeze, especially if it is unilateral or localized; patients whose x-rays show a shadow suggestive of a tumor mass; patients presenting a pneumonic process which does not clear rapidly, that is, within two or three weeks; patients presenting unusual shadows within the lung, whether producing symptoms or not; all patients with a chronic cough, particularly males over the age of forty, and especially the smokers or those in whom the cough has changed in character recently; patients presenting a history of hemoptysis, even of small amounts; and all patients with an unexplained pleural effusion, especially if it is bloody in character.

Treatment. The treatment of primary bronchogenic carcinoma is primarily surgical if conditions are favorable and the risk legitimate. Failing in this, radiation treatment, intravenous nitrogen mustard and the use of some of the radio-active substances may be tried with diminishing chances of success. Surgical treatment for primary bronchogenic carcinoma must be radical, most usually total pneumonectomy with hilar and mediastinal node dissection. The best results thus far produced have followed this type of treatment. Primary bronchogenic carcinoma is an extremely serious condition. In a group of 443 patients presented by Buchberg, Lubliner and Rubin not treated surgically, 84.2% died within 2 years of the onset of symptoms. 15.8% lived from 2 to as long as $7^{1}/_{2}$ years, 7 living 5 years or longer. Patients with epidermoid carcinoma lived the longest and those with anaplastic carcinoma the shortest, and those with adenocarcinoma falling in between. The 5 year survival rate was then 1.5%. The 5 year results following surgical resection have been variously reported at from 19 to 23%.

There are occasional patients presenting a localized tumor with no demonstrable lymph node involvement who have been treated by lobectomy who have likewise survived 5 years or more. Theoretically, at least, there should be a time in bronchogenic carcinoma when such an operation, or even local excision, should produce a cure. If the tumor is yet a local process with no invasion of the lymphatics or vascular spread, simple excision should produce good results. Unfortunately no one knows when such conditions exist and one should not jeopardize the patient's chances of a possible good result by performing an inferior type of operation if the local conditions and the patient's vital capacity and cardiovascular status and other conditions are suitable for the more radical procedure. Lobectomy will still have its place in elderly individuals with a low respiratory reserve, in the earlier strictly localized lesions and as a palliative procedure to relieve suppuration in patients with metastasis which would render the more radical resections futile.

Radiation therapy of bronchogenic carcinoma with the more conventional 200,000 to

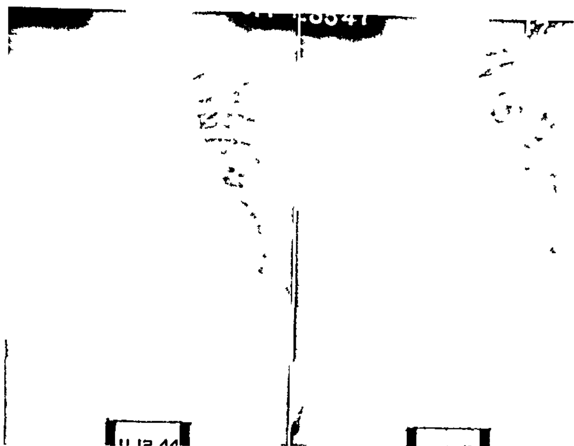


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Radiation therapy of bronchogenic carcinoma with the more conventional 200 000 to

400 000 volt machines has not proven curative in bronchogenic carcinoma though some relief of symptoms particularly those of mediastinal or bronchial obstruction have been obtained Whether life has been prolonged or not remains problematical as this varies widely in individual cases More intensive radiation with the super voltage x ray machines of 1 2 and 3 million volts or the more recently developed cobalt bomb radiation has not materially altered this picture though the much higher dosages possible in the latter technique at least appears to produce less reaction on the patient s part The intravenous use of *nitrogen mustard in the treatment of primary* bronchogenic carcinoma has produced temporary improvement in some patients but the effect is palliative rather than curative Symptomatically however some patients appear to be better It is doubtful that life is prolonged in any

Criteria of Operability of Bronchogenic Carcinoma

Although there is much variation of opinion as to what constitutes operable carcinoma of the lung the following may be taken as a rough guide to conditions apparently favorable for resectional treatment in bronchogenic carcinoma The exact status of all patients cannot be accurately determined prior to exploratory thoracotomy and no patient presenting a reasonable possibility of having resectable tumor should be denied his chance without exploration Conditions favorable for exploration may be listed somewhat as follows (1) There must be no distant metastasis (2) The tumor must lie sufficiently far down the main bronchus so that it may be cut and sutured without encroaching upon tumor tissue (3) There must be no evidence of direct extension into the chest wall or mediastinum nor should there be free fluid in the pleural cavity certainly not fluid containing malignant cells (4) The patient s age and cardiovascular renal status must be such as to present a reasonable likelihood that the patient may tolerate the projected surgery (5) The patient s respiratory reserve must be such that he can tolerate the loss of the one lung and yet retain vital capacity sufficient to carry on afterwards without being a respiratory cripple

Even if such criteria are followed a considerable number of patients at exploratory thoracotomy will be found to present local conditions which render the lesion absolutely unresectable or nonresectable with any hope of cure The use of intrapericardial ligation of the pulmonary vessels will increase the resectability rate but it is uncertain how much it will improve the late survival rate

Criteria of Inoperability

The findings in the individual case may be *such as to preclude any possibility of surgical* control of this condition Unfortunately many patients are seen at a late stage of the disease when they are totally unsuitable for surgical attack In this category are (1) persons with distant metastasis to the brain liver skin spine or other distant sites, (2) patients with tracheal involvement or involvement of the proximal bronchus which could not be sectioned without going through carcinomatous tissue (3) patients with mediastinal obstruction tracheoesophageal fistulae and cervical lymph node involvement Perhaps also in this category should be included vocal cord paralysis and the majority of those presenting hemidiaphragmatic paralysis (4) Patients with pleural effusion and certainly those in which malignant cells can be demonstrated Even if tumor cells cannot be found the presence of a pleural effusion is a very unfavorable finding (5) Patients of advanced years with poor cardiovascular function low vital capacity which would not permit resection with any hope of survival

MALIGNANT MESOTHELIOMA

Years ago many references were made to primary endothelioma of the pleura It is now recognized that this term included a number of cases of extensive pleural involvement from primary bronchogenic carcinoma while others were from the pleural metastasis of hypernephroma and other malignant tumors There is a primary malignant tumor malignant mesothelioma apparently of mesothelial or pleural origin which manifests itself as diffuse

malignant involvement of the pleura usually parietal with less involvement of the visceral accompanied by pleural pain and effusion usually of bloody character and in which malignant cells can only occasionally be demonstrated The condition may be more localized and present as a local tumor mass but this is very unusual This process is easily confused with secondary malignant involvement of the pleura as above mentioned and can usually not be easily separated except by careful microscopic study It does not lend itself to surgical intervention and is usually resistant to radiation therapy

SUPERIOR PULMONARY SULCUS TUMOR (Pancoast)

The Pancost syndrome of an upper thoracic density with erosion of adjacent ribs or vertebral bodies a Horners eye syndrome and pain paralysis and atrophy of the muscles of the shoulder girdle from malignant invasion of the lower portion of the brachial plexus is now well recognized in clinical medicine The term Pancoast tumor is not proper however as the syndrome is not always produced by a single tumor as Pancoast originally believed but may be produced by any infiltrative process occurring in this area Most commonly it is a result of a high peripherally placed bronchogenic carcinoma with direct chest wall invasion but may be produced by a lymphoblastoma a metastatic tumor in this same location or even by a progressive aneurysm The syndrome is produced by invasion and destruction of local structures in the upper portion of the pleural cavity including rib or vertebral body or both interruption of the sympathetic nerve trunk and invasion and interruption of the lower trunks of the brachial plexus The syndrome may be complete with all phases represented or it may be partial with some facets missing depending upon the extent and duration of the process By the very nature of the underlying process the condition is with very rare exceptions a hopeless one from the surgical standpoint and unfortunately except in the case of the rare lymphoblastoma in this region the response to radiation is not usually particularly favorable

SARCOMA

Primary sarcoma of the lung is an exceedingly rare condition Originally it was not thought to exist and was later confused with oat cell and small cell tumors now recognized as of epithelial origin and for this reason the earlier literature is very confused Fibrosarcoma lymphosarcoma leiomyosarcoma lipomyxosarcoma angiosarcoma and malignant giant cell sarcoma have been reported The tumors are not confined to any age group sex or any particular region of the lung They present themselves very much the same as primary bronchogenic carcinoma the diagnosis being a microscopic rather than a clinical one A few cases have been diagnosed from bronchoscopic biopsy material Treatment is the same as for primary bronchogenic carcinoma with excisional surgery offering the best results if conditions are favorable Radiation therapy apparently is not particularly valuable except in lymphosarcomas

BRONCHIOLAR CARCINOMA (Alveolar Cell Carcinoma)

Bronchiolar carcinoma commonly and incorrectly called alveolar cell carcinoma is one of the rarer forms of pulmonary malignancy Earlier it was considered to be multicentric in origin but there is now increasing evidence that it probably begins locally and spreads rather slowly through lymphatics and bronchi to adjacent tissues and then to other lobes on both the same and the contralateral side eventually showing both local and distant metastasis The earlier reported studies made on patients late in the course of the disease suggested a multicentric origin of the tumor More recent recognition of the earlier stages of this lesion show quite conclusively that it apparently starts as a local lesion and spreads at a rather slow rate eventually filling up most of both lungs the patient often dying from lack of breathing space rather than from metastasis Available information would apparently suggest that it begins as a small nodule peripherally located and not in the alveoli or in the major bronchi hence the term bronchiolar carcinoma For this reason bronchoscopic

examination may be of little value in diagnosis, even in the presence of extensive involvement

It presents no characteristic age or sex preference and no typical symptom complex to suggest the nature of the condition The x-ray picture early is that of an isolated nodule in the lung and late may give the characteristic picture of multiple nodulations bilaterally placed which may suggest the diagnosis but which is usually confused with pneumoconiosis, capillary pneumonitis or multiple metastatic lesions Profuse mucoid sputum, once thought to be characteristic of this condition, may be so only in the later stages and even then may not occur Hemorrhage is rare though blood-streaked sputum is common The most consistent finding of any type in this condition is the presence of malignant cells in the sputum or bronchial aspirated material, at times in such great numbers as to raise the question whether they can possibly be malignant

The clinical course of the disease is frequently much slower than in other types of primary malignancy of the lung, and may extend over a period of 3 to 4 years There is no satisfactory treatment for the later stages of the disease. If it is diagnosed early in the operating room following the removal of an isolated pulmonary nodule a lobectomy with node dissection should be carried out at once for this offers the best chance for good clinical results An increasing number of favorable results under such circumstances are now appearing in the literature

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CHAPTER 20

Chest Injury

NATHAN KENNETH JENSEN, M.D.

INTRODUCTION

PHYSIOLOGICAL and bacteriological considerations separate chest injuries into penetrating and nonpenetrating, depending upon whether the parietal pleura has been disrupted by an object traversing the full thickness of the chest wall. Penetrating wounds are further subdivided into open and closed types. Open penetrating wounds result in a vicarious air way into the pleural space and the production of a sucking wound. Closed penetrations do not produce sufficient defects in the chest wall to create sucking wounds but are frequently followed by pneumothorax and hemothorax, the blood most often coming from the chest wall and the air from a rupture of the lung.

Penetrating wounds are common in war but are seen much less frequently than nonpenetrating injuries in civilian life. Except for the gunshot wounds that occur as a result of police action or as hunting accidents, most penetrating wounds of civil life occur as a complication of a crushing injury such as that sustained in a motor accident where a part of the vehicle is forcibly driven through the chest wall.

Because of this frequency of occurrence, nonpenetrating injuries will be discussed first. Most of the physiological considerations of a crushing injury apply equally well to penetrating injuries except for the problems presented by a sucking wound.

NONPENETRATING CHEST INJURIES

Nonpenetrating chest injuries vary in severity from superficial abrasions to massive crushing injuries causing instant death from rupture of the heart or great vessels. Minor chest injuries are very common and have a wide variety of causes, varying from the usual falls about the house to tumbles on icy streets, the jostling of passengers in a vehicle suddenly stopped by a minor collision or emergency brake action, to the snapping of a feminine rib or costochondral cartilage by a vigorous masculine embrace. Even violent coughing occasionally snaps a rib. Most of these injuries can be treated expectantly with good results. Strapping, whether with adhesive tape or elastic support such as is provided by an Ace Bandage or Elastoplast, is worthwhile if it adds to the comfort of the patient; otherwise it has no virtue and should not be persisted in.

Even these simple injuries are occasionally fraught with serious and troublesome sequelae. A fractured rib is a sharp structure capable of lacerating the lung and causing a pneumothorax or tearing an intercostal artery and producing a fatal intrathoracic hemorrhage. These hazards exist for several days after the fracture has occurred until absorption of bone has dulled the fracture ends (Fig. 9). A single rib fracture will also restrict respiration on the injured side and limit effective coughing (Fig. 1). Thus the stage is set for retention of bronchial secretions, atelectasis, and obstructive pneumonitis or, in the older terminology, "rib fracture pneumonia."

A most troublesome complication is costochondral separation or fracture of a costo

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EFFECT OF INCREASING RATE OF VENTILATION

Rate per min.	Tidal Volume (Depth)	Minute Volume Dead Space	Minute Volume Alveolar	Total Minute Volume	Efficiency of Ventilation
20	350	4000	3000	7000	43%
40	350	8000	6000	14000	21.5%

EFFECT OF INCREASING DEPTH OF VENTILATION

Rate per min.	Tidal Volume (Depth)	Minute Volume Dead Space	Minute Volume Alveolar	Total Minute Volume	Efficiency of Ventilation
20	350	4000	3000	7000	43%
20	700	4000	10000	14000	71%

proximately 200 cc. of ventilatory dead space between the nose and the alveolus, the effect of rate and depth on alveolar ventilation is quite different. Shallow breathing at rest is carried on with a tidal ventilation of around 350 cc. per inhalation. Two hundred cubic centimeters of this is lost in the dead space and only 150 cc. alveolar ventilation occurs. As the calculations above show, increasing the rate without deepening ventilation multiplies the dead space in the same ratio as the alveolar ventilation. Although minute volume of exchange is greatly increased, alveolar ventilation suffers in comparison with dead space ventilation.

The above calculations show the efficiency of increasing the depth of respiration in relation to alveolar ventilation. Deep slow ventilation exchanges the air in many alveoli and efficiently accomplishes respiratory exchange whereas rapid shallow ventilation fails.

The flow of blood through the vascular bed of the lung is so regulated that a great bulk of the volume is diverted through alveoli being ventilated. Pulmonary blood flow to nonventilated *portions of the lung is sharply restricted.* This mechanism avoids shunting large volumes of blood from the venous side through resting portions of the lung. If it were not for this arrangement we would all be quite cyanotic except with full pulmonary ventilation.

This relationship between ventilation and pulmonary perfusion illustrates how dependent respiration is on ventilation.

Figure 1 graphically illustrates this. These tracings were made by differential bronchospirometry carried out on a patient with minor rib fractures on one side only. This man was ambulatory and with quiet breathing was in little distress. The lower tracing on the graph recording the respiration on the injured side shows considerably less oxygen uptake per minute despite about the same tidal ventilation. This means that alveolar ventilation was limited to a restricted area of pulmonary tissue on the injured side. As a result this restricted area was being over ventilated and only a limited portion of the vascular bed of this lung was available for respiratory exchange. Auscultation and observation showed costal respiration on the injured side immobilized by intercostal muscle spasm. Ventilation was diaphragmatic with breath sounds heard only at the base. Note (to the left on the record) that with conscious effort deep ventilation could be effected. Midway on the graph spontaneous coughing results in no increased expulsion of air from the injured side. On the uninjured side the pointer is blown off the paper.

These tracings are highly significant for they illustrate the limited and poorly distributed ventilation which occurs on the side of injury. *They also illustrate that with conscious effort* this can be compensated for and finally they illustrate that coughing on the injured side is noneffective. It is immediately apparent from these tracings why heavy sedation is dangerous to patients who have suffered chest injuries. Conscious effort at ventilation can overcome the splinting of the injured chest wall. If consciousness is obtunded this action is lost. These tracings also illustrate that ventilation on the injured side is poorly distributed and greatly limited with perfusion through the lung markedly reduced.

Two factors have a primary role in this re

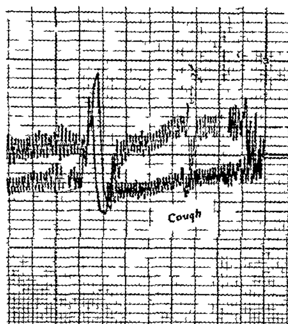


Fig 1 Tracings of differential bronchospirometry Young male with single rib fracture Lower tracing is of injured side Slope of tracing measures oxygen uptake Note at left of tracing deep voluntary inhalation by injured side and intact side are equal By contrast little air exchange occurs on injured side with cough while uninjured side blows pointer off paper Discussion in text

chondral cartilage These injuries frequently occur with surprisingly little trauma They are exceptionally painful and as cartilage does not regenerate they heal slowly A fair number fail to stabilize resulting in exquisite pain localized to the area of the injured cartilage but referred into the pectoral muscle group and shoulder causing serious disability These lesions can be accurately diagnosed by careful firm palpation of the costochondral cartilages localizing the painful area Frequently the fractured cartilage will be softer on palpation and occasionally the examiner can reproduce the click or crunch of which the patient complains and trigger the excruciating pain of this lesion Shoulder action which puts tension on the pectoral group of muscles frequently produces the pain of this lesion Coughing deep breathing and straining to lift or at stool commonly causes pain These lesions have been mistaken for angina idiopathic pleurisy and commonly in industrial cases for compensation neurosis Careful history and meticulous physical examination will avoid these errors Treatment is at first expectant with explanation to the patient of the nature of his difficulties and the further explanation that the lesions heal slowly Reassurance must be given that although the pain is agonizing it is not harmful emphasizing that nothing vital is being torn apart despite the excruciating pain If no improvement has occurred in four to six months the involved cartilage must be excised taking great care to leave the perichondrium intact and to remove every bit of the cartilage exposing raw cancellous bone at the sternum and rib end If the perichondrium is left intact and not torn up by the procedure it will regenerate bone which will establish a firm and painless union between the sternum and the rib end

Serious crushing injuries of the chest result in profound disturbances in the physiology of respiration Both ventilation and perfusion of the lung suffer These injuries cannot be properly understood or evaluated unless the nature of the physiological disturbance is clearly visualized by the physician Serious chest injuries cannot be treated by the "cook book method but must be handled individually on the basis of the physiological and anatomical disturbances which have occurred in each case

PHYSIOLOGICAL CONSIDERATIONS

Respiration has two functions Both are equally important Oxygenation is understood by laymen and profession alike because of clinical availability and the color changes which occur on the body surfaces with hypoxia Respiration has an equally important function in the removal of carbon dioxide Oxygenation and the elimination of carbon dioxide require the same degree of ventilation of the pulmonary alveoli and the same degree of circulatory perfusion of these alveoli If respiration is failing as evidenced by cyanosis carbon dioxide elimination is also imperiled as evidenced by hyperpnea or dyspnea Both ventilation and perfusion of the lungs are disturbed by severe crushing injuries of the chest

Ventilation of the lungs varies both in rate and depth Because of the existence of ap

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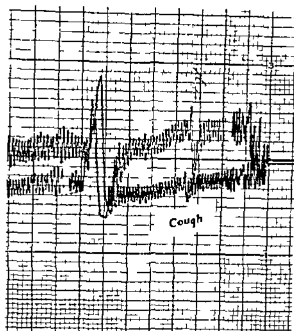


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ant rigid immobilization of the rib cage. Figure 2 is a classic illustration of such an injury.

This is a young woman who, in a motor accident fractured her right clavicle, injured her right cervical plexus, but failed to fracture a rib. The roentgenogram was made 1 hour after injury. Note the marked pulmonary edema in the upper lung fields with the clear areas just above the diaphragms where ventilation is still occurring. This woman was in marked hyperpnea with severe cyanosis at the time this film was made. The pulmonary edema was clinically evident by diffuse wet rales over both upper lung fields and the presence of pink froth on lips.

We have seen severe acute pulmonary edema in an 18 year old girl who, in addition to a severe crushing injury of the chest again without rib fracture, sustained bilateral fractures of the transverse processes of the first three lumbar vertebrae. These lumbar fractures were accompanied by an extensive retroperitoneal hematoma with spasm of the abdominal musculature. A rigid abdomen immobilizes the diaphragms and the combination of an abdominal injury with spasm of the abdominal musculature accompanying crushing of the thoracic cage results in the most severe crippling of respiration. These patients can only effect rapid shallow respiration. Pulmonary edema follows quickly.

TREATMENT OF TRAUMATIC WET LUNG

The treatment of this type of pulmonary edema requires two things. Oxygen is a specific, for with high oxygen content in the inhaled air even poorly ventilated alveoli receive enough oxygen that perfusion begins to occur through their capillary bed and a more adequate vascular bed through the lungs is created.

With the drop in pulmonary blood pressure the hydrostatic pressure in the pulmonary vessels is well below its osmotic pressure and excess fluid is rapidly absorbed from the lung. The oxygen deficit in this situation is also much higher than the carbon dioxide retention for carbon dioxide perfuses through liquids better than oxygen does and thus a wet lung is able to excrete carbon dioxide more efficiently than absorb oxygen.

In all chest injuries oxygen should be administered by nasal catheter, the tip of the catheter being placed at the level of the uvula (Fig. 3). Oxygen delivered here gives a much better saturation in the alveolus than oxygen administered in the nose and the flow of oxygen also washes out the upper airway during exhalation and materially reduces the respiratory dead space. Oxygen flows of 6 liters per minute through a catheter properly placed in adults is 6 liters per minute.



Fig. 3. [illegible]

Reproduced through the courtesy of Dr. Alvan L. Barach and [illegible] Barach and [illegible] CIPLES AN[illegible] THERAPY IN GENERAL PRACTICE Vol. I, pp. 110 (1940), edited by Dr. David P. Barr.

duction of alveolar ventilation and its poor distribution One is limitation of motion of the chest wall The second is retention of secretions in the tracheobronchial tree due to ineffective cough mechanism As we have seen above this reduction in alveolar ventilation also results in a reduction in perfusion through the lung actually greater than the tidal volume on the injured side would seem to indicate for a good share of this tidal volume is due to over ventilation of the remaining functioning alveoli

Since World War I pulmonary edema has been recognized as a constant accompaniment of severe chest injuries The term traumatic wet lung" was coined at this time but it was not until the fundamental observations of Motley Courand and associates in 1947 that an understanding of the cause and nature of this pulmonary edema was gained Earlier Drinker had shown that hypoxia regularly produced pulmonary edema in experimental animals Just how this caused edema was not elucidated Motley and Courand demonstrated that hypoxia produced pulmonary hypertension and *with pulmonary hypertension* pulmonary edema follows The pulmonary edema complicates the problem for it adds to the amount of secretion already retained in the tracheobronchial tree These secretions *in turn close off more small bronchi* and progressively reduce the amount of alveolar tissue available for ventilation Respiration then becomes more and more shallow with compensatory increase in rate which in turn uses more *oxygen produces more carbon di*oxide and is progressively less effective This is the vicious cycle which literally drowns the patient in his own plasma and bronchial secretions

For the management of this problem there are no magic words nor elixirs in bottles nor potions in syringes Adequate ventilation must be re-established Consideration of the anatomical features of these injuries points the way in each case to the re establishment of effective alveolar ventilation

ANATOMICAL CONSIDERATIONS

Factors which determine the nature and extent *of the anatomical disorganization of a* crushing injury of the chest are the force and direction of the impact and the age and sex of the victim Young people have much more flexible ribs than older people Females have *more flexible ribs than males* Children and young females can sustain enormous distor*tions of the thoracic cage without fracture of* ribs These distortions however do severe damage for although the ribs may not be broken the distortions are well beyond the range of the intercostal musculature This is disrupted and thrown into spasm with result



Fig 2 Roentgenograms *of young female showing* severe pulmonary edema developing immediately after crushing injury of chest Film at left taken one hour after injury Subsequent films show clearing of edema No ribs fractured

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Fig 3 Placement of oxygen catheter Nasal position (A) much less effective than nasopharyngeal (B) Catheter tip placed lower in pharynx than at tip of uvula will result in gastric distention from swallowed O Optimum rate of flow for adults is 6 liters per minute

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the nasal pharynx will give an alveolar saturation of *around 70%*

The next step in treatment of this type of traumatic wet lung is tracheobronchial aspiration Spray cocainization of the larynx allows the intratracheal introduction of a suction catheter with a direct vision laryngoscope This catheter can be advanced into both bronchi If the head is turned to the right, *it will go into the left main bronchus If it* is turned to the left, the catheter will go into the right main bronchus The catheter can be moved back and forth and with good suction the secretions removed from the major bronchi and trachea Catheter motion will stimulate coughing which will be effective despite the injury and will bring more fluid to the catheter tip Suction should not be persisted in for long periods at any one time but should be repeated until the tracheal and bronchial rhonchi are cleared The alveolar fluid will be reabsorbed by the pulmonary circulation as its pressure drops towards normal with increasing ventilation and adequate oxygen therapy

Occasionally nasal oxygen and tracheobronchial suction alone will not reverse the pulmonary edema in these cases It is well to remember that one is dealing with a respiratory emergency and simply ordering nasal oxygen and suction to be carried out by a confused house staff will not accomplish the job The responsible physician must stay on the job until it is certain that the pulmonary edema is subsiding and respiration is becoming deeper and a clear airway has been assured It may be necessary to promptly in*tubate such a patient* with a cuffed tube through which positive pressure can be delivered Oxygen then can be delivered from a standard anesthetic machine by bag pressure in rhythm with the patient's respiratory motion This is best done by a skilled anesthesiologist but can be carried out by a well trained anesthetist Where we have not been able to establish rhythmic assistance of the patient's respiration we have not hesitated to use enough anesthetic agent to obtund the pulmonary reflexes Occasionally we have used curare or Flaxedil to allow enough relaxa*tion of the respiratory musculature to permit* the anesthetist to take over the ventilation completely In this manner ventilation can be deepened and more alveoli brought into action and the pulmonary edema reduced

MANAGEMENT OF MULTIPLE RIB FRACTURES

Multiple rib fractures are the rule in severe crushing injuries of the chest A rib attached to the spine *behind* and *the* sternum *in front* in paired fashion with its fellow forms a ring This is a brittle ring and it breaks at two points as does any brittle ring One series of fractures occur posteriorly just lateral to the angle of the ribs The other series of fractures is in front at the level of the mid clavicular line Where the fractures are *multiple, a large segment* of the chest wall loses its stability and becomes flail This portion of the chest wall will then bulge out on exhalation and suck in *on inhalation moving* paradoxically with normal respiratory motions This adds greatly to the dead space of ventilation and a great deal of ventilatory effort is expended sucking the chest wall in and pushing it out again rather than sucking air into the lungs on inhalation and exhausting it from the lungs on exhalation Traumatic pulmo*nary edema occurs and bronchial obstruction* follows Coughing efforts are ineffective for they only move the chest wall in and out rather than expel secretions from the lung (Fig 4)

The first step in the control of a flail chest wall is reduction in the resistance to air flow of exchange The narrow point in the airway is at the vocal cords which widen on inspiration and narrow on exhalation This narrowing increases the intrathoracic positive pressure of exhalation which pushes the flail *chest wall out* On the next inhalation it will be sucked back in Much chest wall motion is produced but little air exchanged

The establishment of a large tracheostomy (number six or eight tube for an adult) greatly reduces the resistance of flow in the

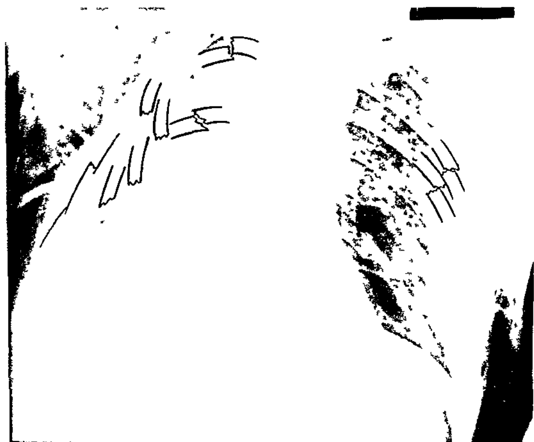


Fig 4 Roentgenogram of severe crushed chest. Many ribs fractured on both sides. Left side stable because of locked rib ends (see lined in ribs). Right side flail as rib ends over ride. Pneumothorax on right with corrective suction catheter in pleural space. Subpectoral emphysema outlines muscles.

airway. It also reduces the dead space by about one half and makes shallow respiration more effective in terms of alveolar ventilation. This reduces the tendency for a flail chest wall to move independently. The tracheostomy also provides an easy access to the tracheobronchial tree for suction removal of secretions and an excellent avenue for administration of oxygen.

In severe bilateral crushing injuries where both sides have become flail a tracheostomy frequently will not suffice. For these cases we have adopted apparatus developed by Frederic J Kottke* for administration of intratracheal oxygen under slightly positive pressure. This apparatus* is illustrated in Figure 5. In its bare essentials it consists of a source of well humidified oxygen with a ten liter elastic collecting bag. The oxygen is led to the tracheotomy tube through a wide corrugated tube containing a one way valve. This prevents rebreathing into the tube. The exhaust is led through wide tubing to a jar where the end is placed under one to four centimeters of water depending upon the amount of positive pressure found necessary to stabilize the chest wall.

A crushed chest accompanied by abdominal

* Professor and Head, Department of Physical Medicine and Rehabilitation, University of Minnesota, Minneapolis, Minnesota

* Available from Medic Made Mfg Co, 202 Peninsula Rd, Minneapolis 27, Minn

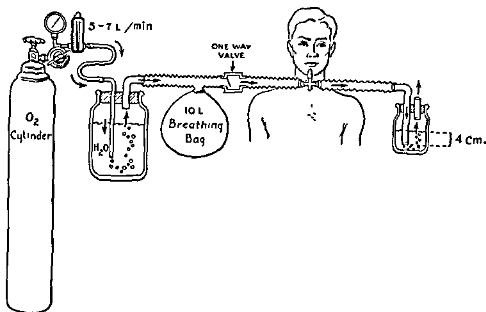


Fig 5 Diagramatic illustration of Kottke apparatus T tube attachment slips into spring clip soldered onto inner cannula In this position it is free to rotate thus allowing tracheotomy tube to maintain alignment in trachea free of torsion from changing positions of large delivery and exhaust tubes Upper opening in T tube, normally capped by

plastic so function can be observed

injury which immobilizes the abdominal muscle by spasm cannot be managed by tracheotomy and positive pressure intratracheal oxygen Mechanical ventilation must be provided, for without abdominal muscles functioning with the diaphragm ventilation against intratracheal positive pressure is impossible Continuous intratracheal positive pressure provides the force of inhalation The contraction of the abdominal muscles pushing the diaphragms back into the thorax accomplishes exhalation If abdominal muscles are rigid the diaphragms cannot move, and if costal respiration is lost by multiple rib fractures no motive power for ventilation remains

Mechanical ventilation can be carried out by intratracheal intubation with a cuffed tube and manual compression of the breathing bag of a standard anesthetic machine This is only an emergency procedure as a cuffed tube soon causes tracheal damage and manual compression of an anesthetic bag soon exhausts available personnel If mechanical respiration is to be maintained for several days a non-cuffed tracheotomy tube will function adequately if connected to a mechanical ventilator having sufficient stroke volume to compensate for gas wastage about the free tube

Most ventilators developed for anesthetic assistance can be used if they have sufficient stroke volume A negative pressure phase is not required and may aggravate a flail chest The simple sturdy piston respirator developed by E Trier Mörch* is ideally suited for this situation (Fig 6)

Avery, utilizing the Morch respirator, has shown that establishment of mild hypocarbia

* Professor and Director, Department of Anesthesia, University of Chicago Clinics, Chicago, Illinois

MOTOR
VARIABLE SPEED
VARIABLE CRANK
PISTON
CYLINDER
HUMIDIFIER
PATIENT
AIR INTAKE → FILTER →
CHECK VALVE
OXYGEN

Fig. 6. Diagram showing the principles of the Morch Piston respirator.

Paradoxical Motion of Flail Sternum

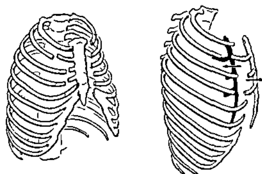


Fig. 7. Diagram illustrating flail sternum due to bilateral anterior rib fractures and costochondral separations.

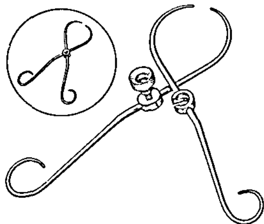


Fig. 8. Kinsella sternal traction tongs.

by slight over ventilation produces apnea in these patients. This allows effective prolonged ventilation without effort by the patient and excellent stabilization of the chest wall results.

Crushing injuries which cave in the sternum and anterior chest wall cause bilateral fractures involving the anterior ends of the ribs and costochondral cartilages. The sternum may not be fractured but usually is. When the sternum is intact it rotates on the clavicles and is sucked deeply into the chest with each inspiration and bulges forward markedly with each exhalation. If a transverse fracture of the upper portion of the sternum occurs the fracture line becomes the point of rotation. This injury is very disabling as the paradox is great and interferes with respiration and venous return to the right side of the heart (Fig. 7).

This is the only injury of the chest where we have found traction useful Traction may be applied in various ways Through short incisions placed adjacent to the sternum a loop of stainless steel wire may be easily passed behind the sternum The best sternal traction tongs are those designed by T J Kinsella as shown in Figure 8 These are easily applied as they come apart at the lock and each half can be slipped into place with its point behind the sternum Then the forceps are locked in position with the knurled nut It is well to remember in applying traction to the sternum that the internal mammary artery runs about a centimeter and a half lateral to the edge of the sternum Incisions placed at the edge of the sternum do not hazard this vessel

Traction of two to four pounds is applied by pulleys attached to an overhead frame It must be maintained for about 10 days then gradually reduced over the next week Several days after stability has been obtained one may release the traction for brief periods to allow the patient bedside bathroom privileges and for upright portable x rays However if the traction is abandoned for any prolonged period at this time the soft fixation of the chest wall and sterum soon breaks down due to respiratory activity and paradoxical motion recurs Stabilization requires two to three weeks

TRAUMATIC PNEUMOTHORAX

Pneumothorax is frequent in chest injuries with fractured ribs The fractured rib ends are initially very sharp and often lacerate the lung at the time of injury producing an immediate air leak When left exposed by disruption of endothoracic fascia and parietal pleura the jagged ends come to rest against the lung and soon cut the visceral pleura producing an air leak Frequently coughing or turning will expose a fractured rib several hours to several days after the injury and thus lacerate the lung producing a delayed pneumothorax This is a complication for which one must be continually on the watch particularly in those injuries where multiple rib fractures have occurred and a portion of the chest wall has abnormal mobility

Subcutaneous and chest wall emphysema is a frequent accompaniment of traumatic pneumothorax The rib fractures have disrupted the endothoracic fascia and the parietal pleura and air collecting in the pleural space readily infiltrates through these areas into the musculature of the chest wall and then into the subcutaneous tissue (Fig 4) The air spreads centrifugally through the tissues advancing more rapidly in the areas where tissue planes facilitate its migration Gross distortion of the neck and axillae is common Wide spread dissemination of the air occurs rapidly and frequently air reaches the soles of the feet This subcutaneous and interstitial air although alarming to the patient causes relatively little trouble unless it accumulates in such quantity as to interfere with function by mechanical pressure Decompression of the pleural space by an air leak into the chest wall unquestionably has saved the life of many patients who otherwise would have died of a tension pneumothorax

Mediastinal emphysema may arise either from a rupture of the mediastinal pleura at the time of the injury and subsequent decompression of a traumatic pneumothorax into the mediastinum or less commonly it arises without accompanying pneumothorax due to rupture of the pulmonary parenchyma adjacent to the vascular sheaths which accompany the blood vessels into the lung as originally pointed out by Macklin The air dissects along the vascular sheaths into the mediastinum and in turn follows the vascular structures out of the mediastinum This latter also occurs when the air enters the mediastinum through torn mediastinal pleura As a result with mediastinal emphysema we find the palpable crepitation of interstitial air appearing first along the carotid vessels and in the axillae Before air is palpable along the vessels one can hear the characteristic sound of gaseous crepitation by auscultation over the sternum Mediastinal air may become

widely disseminated and it may also produce severe embarrassment by progressively compressing the superior and inferior vena cava and obstructing the inflow tract to the heart Mediastinal emphysema collecting rapidly and causing early embarrassment suggests rupture of the trachea or one of the bronchi or the esophagus Under these circumstances the parietal pleura is soon disrupted by the accumulating air and pneumothorax develops on either or both sides

Extensive interstitial and subcutaneous emphysema will occur without the development of a pneumothorax if firm obliteration of the pleural space exists Here when the lung is ruptured by a sharp rib end the air leak occurs directly into the soft tissue of the chest wall and although infiltration may extend quite widely little respiratory embarrassment results Occassionally the adhesions obliterating the pleural space are quite filmy and with infiltration of this space gradual disruption of these adhesions occurs and a true pneumothorax develops

The diagnosis of a pneumothorax is difficult and is frequently missed The reasons are obvious If the intrapleural gas is under positive pressure breath sounds are transmitted from the underlying lung or from the opposite lung with surprising clarity Not infrequently one is amazed at how loud and close to the chest wall the breath sounds are with a collapsed lung Due to loss of chest wall structure by multiple rib fractures and traumatic edema the characteristic percussion note of pneumothorax is dampened until it may be more characteristic of fluid than air Thus the two most commonly used physical signs can not be relied upon

If the pneumothorax is unilateral and producing mediastinal shift palpation for the position of the trachea in the suprasternal notch will reveal the shift quite reliably This should be one of the first maneuvers in the examination of a patient with an injured chest

Contrary to common opinion a pneumothorax is hard to demonstrate by x ray The characteristic roentgenogram showing the collapsed lung surrounded by a zone of air is a photograph of a certain situation and one cannot expect to obtain this photograph unless the requirements of the situation are met This is a postero anterior film taken with the patient in the upright position and taken with short enough exposure time to stop respiratory motion A supine AP film will frequently fail to demonstrate a large pneumothorax because in the supine position the lung falls back in the thorax and flattens out contouring itself to the posterior half of the thoracic cage Thus when a supine x ray is taken the tracery of pulmonary parenchyma occurs uniformly over the film even on the injured side It is only when the patient sits up that the lung falls away from the chest wall towards the mediastinum AP films even upright are unfamiliar to most of us and cannot be reliably interpreted except in the simplest situations

Because of the urgency of clearly demonstrating a pneumothorax or a pneumohemothorax or a hemothorax in the presence of a crushing injury of the chest we insist that an upright PA film taken at a tenth of a second or less be promptly obtained on all admissions who have sustained chest injuries We feel that is so important that we willingly let the patient become cyanotic and sag into shock while supported by two strong members of the house staff to get the required roentgenograms These pictures should be made with the attending surgeon present They can best be made from the sitting position with a cassette reaching from the thighs to the chin and the machine placed across the table or the bed giving a PA exposure Six foot films are not essential but again it is necessary to emphasize that short exposures are essential and this usually means that the large stationary equipment in the hospital must be utilized to obtain these films Most portable machines do not have enough gamma ray output to provide the penetration with the short exposure required in a big man breathing 40 times a minute

Only when injuries absolutely preclude obtaining an upright film should one settle for less The best alternative films are obtained with the patient in the lateral recumbent position again with the film shot in the PA projection and with brief enough exposure

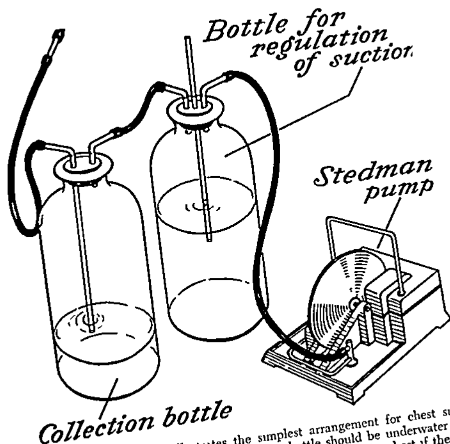


FIG 9 This diagram illustrates the simplest arrangement for chest suction The tube from the chest entering the suction bottle should be underwater 1 cm This allows easy rapid blow off but prevents air re-entering the chest if the pump fails or a leak develops between the jugs or the pump Any pump having sufficient capacity may be used The tube in the suction adjustment bottle should reach under the surface about 14 cm If a pump is not available use the collection bottle with the long tube reaching just below the surface and vent the jug to room air Gallon jugs are the right size

time to stop respiratory motion A pneumothorax or a pneumohemothorax can be well demonstrated by this projection if the side of the lesion is turned uppermost It is well to remember that in obtaining initial films both lateral positions must be used The right lateral recumbent will show the left lung and the left lateral recumbent will show the right lung Interpretation of the roentgen findings on the down side are too unreliable to warrant consideration

The treatment of pneumothorax either spontaneous or traumatic is usually quite simple Emergency treatment requires only the insertion of an 18 gauge needle through the chest wall into the pleural space This needle may be left in position covered with a large cotton ball or a small pasteboard box strapped to the chest It allows life saving decompression of the pneumothorax until more definitive measures may be undertaken As soon as possible this temporary expedient should be abandoned and lung re-expanded to fill the pleural space

We are not enthusiastic about attempts at re expansion by needle aspiration, for as the lung is expanded out against the chest wall the needle invariably will lacerate a new area of pulmonary tissue due to the unavoidable respiratory motion If needle aspiration is to be undertaken a Potain cannula providing a blunt end should be used

In general we have found it much more satisfactory to do a trocar thoracotomy for definitive treatment, placing a two hole Robinson type rubber catheter which is x ray opaque in the anterior upper chest This catheter is

attached to an underwater seal or a pump adjusted to provide constant negative pressure of not over 20 cm of water. One catheter will usually suffice if no fluid is present in the pleural space; however, if fluid is present a second catheter should be inserted and directed posteriorly to lie in the gutter just above the diaphragm. Catheters are best inserted through the lateral chest wall. They can be directed to any location in the pleural cavity by directing the trocar as it is pushed through the chest wall in the direction one wishes the catheter to follow. The trocar cuts a channel through the chest wall at the desired angle and this channel will subsequently hold a catheter in the same position.

Commonly the small Stedman pump developed originally for suprapubic cystotomies and sold by the American Cystoscope Makers is used for chest suction. This pump has a very limited capacity and frequently the air leak from a ruptured lung is much greater than this pump can manage. It is often necessary to attach several of these pumps in parallel to stay ahead of the leak. When massive air leaks are present it is probably better to use just an underwater seal to allow a very rapid blow off from the pleural space through the catheters during exhalation.

HEMOTHORAX

Intrapleural hemorrhage like pneumothorax may be either early or late. Most frequently the hemorrhage occurs immediately following injury and some fluid is demonstrated in the initial x-ray films taken at the time of admission. However, when deep inspiration is difficult a fair amount of fluid may be hidden in the costophrenic angle and not appear in the x-ray film. Thus a patient can readily have bled a thousand cc into the pleural space and this fluid not be apparent in an upright film taken without deep inspiration. Lateral decubitus films will show the fluid earlier. If pneumothorax is present an upright film or lateral decubitus will show a fluid level. The physician must never dismiss the possibility of a fatal progressive hemorrhage into the pleural space even though the initial x-ray films show no evidence of such (Fig. 10).

Blood should be removed promptly and completely from the pleural space. Needle aspiration is frequently inadequate and is always somewhat dangerous. As the fluid is aspirated the surface of the lung comes out against the aspirating needle and is readily torn and a pneumothorax results. This is undesirable as lung expanded against the chest wall tends to seal off the bleeding points. If bleeding is active at the time of aspiration it will become more severe following the aspiration if pneumothorax is allowed to occur either by tearing the lung or allowing the air to escape back into the chest through the needle as the aspiration is carried out. If syringe aspiration is to be undertaken it is best to use a Potain cannula and avoid the dangers of a sharp needle point in the pleural space.

Blood accumulating in the pleural space is rapidly defibrinated by motion of the heart and lung much the same as blood in a beaker is defibrinated by a whip. The fibrin is deposited on the pulmonary surfaces and parietal pleura and rapidly organized by the ingrowth of fibroblasts. If the lung be only partially expanded at the time organization occurs, full expansion is subsequently impossible because of the constricting nature of the scar. A clot allowed to remain in the pleural space gradually hemolyzes. With this increase in osmotic pressure it imbibes more and more plasma from the adjacent circulation. This plasma in turn clots and expands as more plasma and fluid are absorbed due to increasing osmotic pressure built up by the progressive lysis of cellular elements. This is the same mechanism as occurs in a subdural hematoma only on a much larger scale and a relatively small hemothorax may grow into giant proportions with surprising rapidity. Blood and air must be aspirated promptly and full expansion maintained.

Early, complete, and continuous aspiration avoids the late complication of clotted hemo-

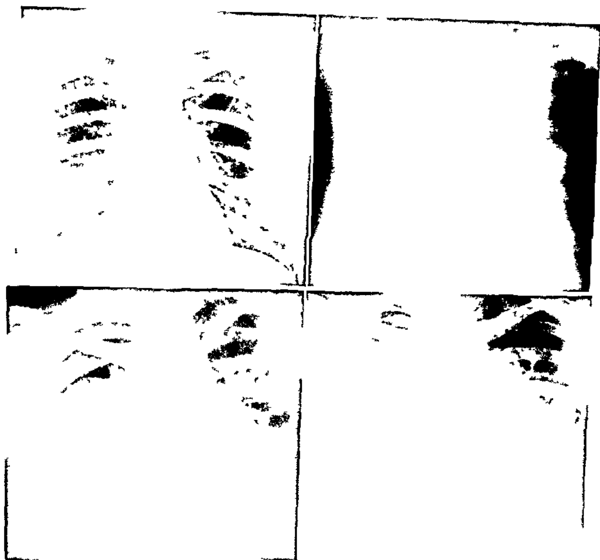


Fig 10 The admission x ray shown in No 1 was obtained several hours after relatively minor crushing injury Patient was ambulatory and in little distress No 2 shows an upright film 12 hours later Patient now in shock despite 1000 cc blood replacement Catheter inserted in right chest at this time and 1800 cc blood removed Large residual clot shown in No 3 Bleeding continued and despite continuous catheter suction removal of blood a huge clot formed shifting mediastinum to left with severe respiratory embarrassment Thoracotomy required to relieve compression shown in No 4 Single lacerated intercostal artery found still bleeding Case illustrates hazard of late severe hemorrhage

thorax Continuous aspiration also provides a good objective measurement of the rate of bleeding Generally speaking one cannot count on aspirating all the blood which seeps into the pleural space from an active bleeder A fair amount of it is defibrinated and caught in the loculi of fibrin despite the presence of multiple suction catheters When the catheters have returned a 1 000 cc of blood there is usually about the same amount in the pleural space some of it still liquid but most of it trapped in the soft syncytium of fibrin Thus if a 1 000 cc of blood has accumulated in the suction bottle and bleeding is still going on even at a slow drip it is best to do a thoracotomy and evacuate the large clot which will be found and control all bleeding points The chest is reclosed with multiple catheters to maintain full lung expansion Likewise if bleeding continues during the initial observa

tion period it should be accurately replaced by whole blood for the amount of blood in the suction jug is considerably less than the total loss from the circulation due to the formation of clots in the pleural space

A delayed intrapleural hemorrhage may occur just as a delayed pneumothorax and by the same mechanism Multiple rib fractures result in a flail chest wall accompanied by excessive abnormal motion at the fracture sites This motion may at any time tear an intercostal artery starting an intrapleural hemorrhage This hemothorax should be treated as outlined above Because of this ever present potential new hemorrhage the circulatory volume in a chest injury must be kept close to normal by replacement When ever there is a question of the adequacy of replacement it is helpful to determine the circulatory volume

FIBRINOTHORAX

Clotted fibrinothorax must be decorticated and the lung re expanded The clot will usually become infected and unless the lung is re expanded a chronic empyema results Decortication is best carried out early before the fibrin deposit over the pleural surfaces has been infiltrated by fibroblasts Within the first week or ten days after the clot forms it is easy to rub the fibrin away with a sponge and re expand the lung without any pleural dam age In about two weeks the fibrin begins to be organized by fibroblastic proliferation and is difficult to remove By 3 to 4 weeks after injury the fibroblastic proliferation has con verted the deposited fibrin into a tough mem brane which can be more readily peeled away from the visceral pleura Thus unless infec tion supervenes with sepsis and toxicity it is better to wait about 3 to 4 weeks following the formation of a hemothorax before decorti cation is attempted unless one has an oppor tunity to evacuate the clot early Decortica tion can be carried out years later but it be comes an increasingly difficult chore

In general it is not worthwhile to decorti cate the parietal pleura as the scar is much thicker there and much greater vasculariza tion has occurred and forceful decortication of the parietal layer when it has become well vascularized may result in uncontrollable bleeding If the lung is re expanded and the pleural pocket obliterated the chest wall scar tissue will gradually be reabsorbed and us able motion regained

RUPTURE OF DIAPHRAGM

Rupture of the diaphragm occurs concomi tantly with crushing injuries of the chest par ticularly when abdominal injury has also been sustained The left diaphragm ruptures much more frequently than the right The rupture may either be through the membranous por tion of the diaphragm or less frequently rup ture occurs through the esophageal hiatus

The ruptured diaphragm presents several problems The immediate problem is rather severe interference with respiration Intra abdominal pressure is always above atmos *pheric pressure depending* upon the tone of the abdominal musculature Intrathoracic pressure is always negative due to the continu ous *elastic recoil of the lung* When the dia phragm ruptures the negative pressure in the hemithorax on that side is immediately lost by displacement of the abdominal viscera into the thoracic cage Mediastinal shift occurs towards the uninjured side and the intra thoracic pressure on that side is reduced This seriously limits the depth of inhalation possible and results in rapid shallow ineffec tual breathing Coughing is limited with a ruptured diaphragm Thus we have much the same situation with a ruptured diaphragm as *with a crushing injury resulting in a flail seg* ment of chest wall

In addition to the respiratory crippling

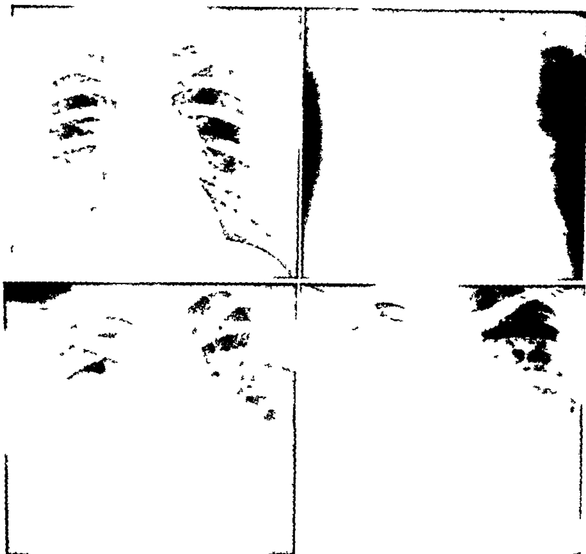


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which results from a ruptured diaphragm, abdominal visceral injury is frequent The most frequent acute injury accompanying a ruptured diaphragm on the left side is rupture of the spleen Traumatic rupture of bowel occurs and strangulation of the stomach and large intestine accompany their incarceration in a diaphragmatic hernia

The diagnosis of diaphragmatic hernia is urgent Adequate upright x-ray films must be obtained to establish this diagnosis When there is any question about the position of the diaphragm it can be easily outlined by the injection of 500 or 600 cc of carbon dioxide* into the peritoneal cavity and upright roentgenograms If the diaphragm is ruptured and plugged by incarcerated viscera it will be beautifully outlined as will the abdominal viscera where it penetrates the diaphragm by the induced pneumoperitoneum If the diaphragm is ruptured but the rupture not closed by incarcerated abdominal viscera, the injected gas will be found at the top of the thorax on the injured side in upright roentgenograms

Rupture of the left diaphragm with fracture of the spleen results in herniation of the fractured spleen into the thorax in almost all instances The rapidly progressing hemorrhage from the fractured spleen will accumulate both in the thorax and peritoneal cavity Characteristically there will be no fluid levels on the upright films of the thorax even if some pneumothorax is present as the fluid drains away into the peritoneal cavity in the upright position

On the right side, however, with rupture of the diaphragm through the bare area liver is always fissured and rapid hemorrhage from the liver may occur As the liver may seal off the defect in the diaphragm the hemorrhage will occur entirely into the right thorax and a large compressing hemothorax develop This blood must be removed to allow re expansion of the lung Persistent bleeding requires exploratory thoracotomy The fractured liver can be managed if it is still attached to the diaphragm and the fracture has not extended through to the peritoneal surfaces by packing the fissure with gelfoam and suturing the diaphragm to compress the liver on the gelfoam If the fissure has extended through the liver into the peritoneal cavity or if additional fissures have occurred in the liver through the peritoneal surfaces these must be dealt with through an abdominal incision or a combined thoraco abdominal

Fractures of the spleen accompanying ruptures of the diaphragm are best dealt with through a thoracic incision The spleen is readily available through the ruptured diaphragm and can be quickly extirpated Then the diaphragm can be repaired at leisure after the hemorrhage is controlled It is well to remember in this connection that an abdominal incision in the presence of a rupture of the diaphragm results in a sucking wound of the chest which demands immediate establishment of intratracheal anesthesia to maintain respiration with positive pressure until the rent in the diaphragm can be closed and air tight integrity of the thoracic cage re established

Repair of a ruptured diaphragm requires suturing in two layers with interrupted cotton or silk sutures so placed that the knots are buried by the imbrication for the lung moves back and forth across the diaphragm on the upper side and the abdominal viscera does likewise on the lower side and the rubbing of these structures against the knots will readily untie them with recurrence of the hernia We have come to prefer cotton here The cotton knot is harder to untie and the cotton tends to cut the diaphragm less with motion One should take care in placing sutures when the rent extends close to major branches of the phrenic nerve not to strangulate a branch and paralyze a large portion of the diaphragm Following the completion of the repair the chest is closed in the usual manner with one or two suction catheters

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* Carbon dioxide is safe to use for diagnostic gas contrast x ray studies If accidently injected intravenously its high fluid solubility protects against gas embolization

INJURIES OF TRACHEA AND BRONCHI

Rupture of the trachea and major bronchi (Fig. 11) occurs with sufficient frequency to deserve consideration. Ruptures of the trachea as a result of trauma to the chest, head and neck occur almost exclusively in the cervical portion of the trachea. The usual mechanism is a direct blow on the trachea associated with hyperextension of the neck so that the trachea is compressed against the cervical spine and at the same time stretched. It usually ruptures between the second and the sixth ring. Most of the ruptures are in

complete Occasionally the rupture is complete with retraction of the distal end of the trachea into the mediastinum

In addition to the local pain accompanying the injury which may be quite over shadowed by the terrific pain occurring elsewhere in the body *from multiple injuries the presence of* a ruptured trachea is immediately signified by rapidly spreading subcutaneous emphysema which develops first in the cervical regions and over the shoulders and then rapidly spreads to the face and trunk Coughing is invariably present and almost always bloody sputum or frothy blood is expectorated. With minor ruptures such as fissure fractures there is little immediate airway obstruction However with extensive rupture and separation dyspnea accompanied by ballooning of the neck with each exhalation is severe The dyspnea may be greatly aggravated even in minor injuries by dissection of the air into the pleural spaces through the mediastinal pleura with the production of pneumothorax

The diagnosis can be readily and quickly made by bronchoscopy if the patient s condition permits *In the case with severe dyspnea* and rapidly spreading emphysema immediate tracheotomy is indicated This exploration of the cervical trachea will reveal the defect We have recently had a patient admitted to the hospital after an automobile accident with severe dyspnea hoarseness bloody harassing cough and marked cyanosis accompanied by rapidly spreading cervical and subcutaneous emphysema

On cervical exploration the trachea was found to be completely separated with the distal end retracted well below the sternum Direct laryngoscopy showed both vocal cords to be paralyzed Repair of the trachea was carried out by trimming the frayed ends and re approximating with interrupted oooo silk A tracheostomy was made in the segment below the repair The patient made a rapid clinical recovery the vocal cords remained paralyzed for three months and only after function returned were we able to remove the tracheotomy tube

Complete ruptures where there is any displacement rapid air leak or separation at the line of disruption require closure with interrupted oooo silk through a cervical incision Incomplete fissures being held in good approximation without appreciable air leak do not require suturing but as in all severe tracheal injuries a tracheotomy should be performed and maintained for approximately three weeks

Penetrating wounds of the cervical esophagus and trachea are not difficult to manage if seen early before softening and further destruction of the tissue has occurred by suppuration Fresh wounds can be closed by primary suture after debridement with good expectation of healing. In esophageal injuries it is best to maintain gastric suction for 3 or 4 days to avoid vomiting as the acid pepsin gastric juice is very destructive of a fresh suture line in the esophagus It is wise to prohibit swallowing for about this same period of time sustaining the patient on intravenous fluids By the fourth or fifth day clear liquids can be started by mouth or the gastric tube can be utilized for a feeding tube and by the end of a week normal swallowing can be allowed If a small esophageal fistula does form it will promptly close if adequately drained

Direct lacerations of the cervical trachea can be closed by tight suturing after debridement and if the esophagus is not concomitantly involved the wound need not be drained When the esophagus and trachea are both involved it is best to drain the esophageal closure with a small Penrose drain and perform a tracheotomy to protect the tracheal suture line from excessive intraluminal pressure with coughing and straining After 7 to 10 days the tracheotomy tube can be removed

Mediastinal injuries to the trachea occur with blast injuries blunt trauma and penetrating wounds They can be readily repaired by primary suture or where the loss of substance is great by dermal grafts supported on a stainless steel wire mesh as described by Gebauer

The maintenance of airway and ventilation in these injuries first on an emergency basis and later during the surgical repair is of utmost importance Complete rupture of the cervical trachea requires immediate cervical incision with intubation of the distal trachea with a cuffed tube Adequate airway

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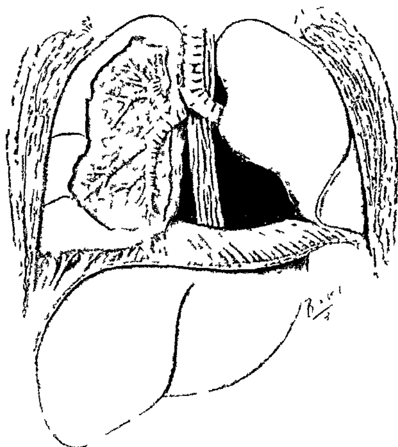


Fig 19 Rupture of bronchus Illustration showing mechanism of traction rupture of right main bronchus due to sudden deceleration producing rapid descent of liver with displacement of diaphragm and traction exerted through existing diaphragmatic pulmonary adhesions

can be maintained while the wound is prepared properly hemostasis obtained and beginning approximation of the two segments started It is then more convenient to remove the tube in the distal segment and re intubate either through the mouth via the larynx or by distal tracheotomy for completion of the anastomosis Incomplete ruptures of the cervical and upper thoracic trachea can be easily handled after bronchoscopy has revealed the extent and location of the tear by the insertion of a cuffed intratracheal tube into the distal trachea thus excluding the injured portion from ventilation until the repair has been completed and a proper cervical tracheostomy established Injuries close to the carina are best handled by intubating the left main bronchus with a long cuffed intratracheal tube This is most easily passed through a cervical tracheotomy allowing the patient to be carried on the left lung using a right thoracotomy for the repair

Traumatic rupture of the bronchus occurs with crushing injuries of the chest

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Complete ruptures where there is any displacement rapid air leak or separation at the line of disruption require closure with interrupted oooo silk through a cervical incision Incomplete fissures being held in good approximation without appreciable air leak do not require suturing but as in all severe tracheal injuries a tracheotomy should be performed and maintained for approximately three weeks

Penetrating wounds of the cervical esophagus and trachea are not difficult to manage if seen early before softening and further destruction of the tissue has occurred by suppuration Fresh wounds can be closed by primary suture after debridement with good expectation of healing In esophageal injuries it is best to maintain gastric suction for 3 or 4 days to avoid vomiting as the acid pepsin gastric juice is very destructive of a fresh suture line in the esophagus It is wise to prohibit swallowing for about this same period of time sustaining the patient on intravenous fluids By the fourth or fifth day, clear liquids can be started by mouth or the gastric tube can be utilized for a feeding tube and by the end of a week normal swallowing can be allowed If a small esophageal fistula does form it will promptly close if adequately drained

Direct lacerations of the cervical trachea can be closed by tight suturing after debridement and if the esophagus is not concomitantly involved the wound need not be drained When the esophagus and trachea are both involved it is best to drain the esophageal closure with a small Penrose drain and perform a tracheotomy to protect the tracheal suture line from excessive intraluminal pressure with coughing and straining After 7 to 10 days the tracheotomy tube can be removed

Mediastinal injuries to the trachea occur with blast injuries blunt trauma and penetrating wounds They can be readily repaired by primary suture or where the loss of substance is great by dermal grafts supported on a stainless steel wire mesh as described by Gebauer

The maintenance of airway and ventilation in these injuries first on an emergency basis and later during the surgical repair is of utmost importance Complete rupture of the cervical trachea requires immediate cervical incision with intubation of the distal trachea with a cuffed tube Adequate airw ay

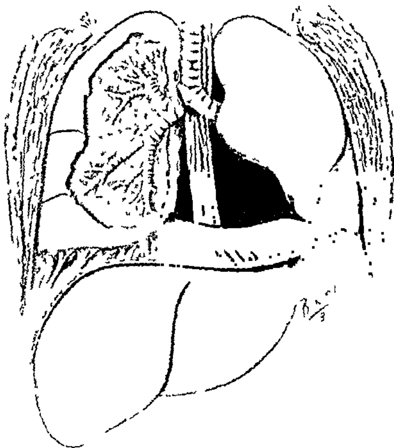


Fig 12 Rupture of bronchus Illustration showing mechanism of traction rupture of right main bronchus due to sudden deceleration producing rapid descent of liver with displacement of diaphragm and traction exerted through existing diaphragmatic pulmonary adhesions

can be maintained while the wound is prepared properly hemostasis obtained and beginning approximation of the two segments started It is then more convenient to remove the tube in the distal segment and re intubate either through the mouth via the larynx or by distal tracheotomy for completion of the anastomosis Incomplete ruptures of the cervical and upper thoracic trachea can be easily handled after bronchoscopy has revealed the extent and location of the tear by the insertion of a cuffed intratracheal tube into the distal trachea thus excluding the injured portion from ventilation until the repair has been completed and a proper cervical tracheostomy established Injuries close to the carina are best handled by intubating the left main bronchus with a long cuffed intratracheal tube This is most easily passed through a cervical tracheotomy allowing the patient to be carried on the left lung using a right thoracotomy for the repair

Traumatic rupture of the bronchus occurs with crushing injuries of the chest either as

a result of direct compression of the bronchus against the spine by deep depression of the sternum or rupture of the bronchus on the right side may occur as the result of sudden deceleration with forceful descent of the diaphragm The right diaphragm is pulled down by the weight of the liver and if diaphragmatic pulmonary adhesions to the right lung exist this traction will disrupt the bronchus at the hilum where the angle of the insertion into the trachea makes it most susceptible to a shearing force (Fig 12)

Such a tear gives an immediate tension pneumothorax which requires prompt decompression by rapid suction through several intrapleural catheters Cervical tracheotomy and bronchoscopic inspection of the tracheobronchial tree delineates the lesion Intubation of the remaining good side with a cuffed tube provides adequate ventilation Thoracotomy on the injured side can now be carried out with immediate repair of the fracture using interrupted silk or cotton sutures not larger than oooo Suture material larger than this will often be extruded into the lumen later on and cause irritating coughing

Following repair of the ruptured bronchus cervical tracheostomy should be maintained for about 3 weeks until healing of the bronchus is complete Tracheostomy allows tracheobronchial aspiration by catheter and the avoidance of atelectasis from retained secretion It also protects the suture line against excessive pressure from coughing and straining

Occasionally in the past such traumatic fractures of the bronchi have survived with just decompression of the pneumothorax A great majority of these have healed with a very tight stenosis of the bronchus at the point of injury In some cases the bronchial closure has been complete and pulmonary suppuration has not supervened In these cases it has been possible to excise the old scar and re anastomose the bronchial segments and regain a functioning lung even years after the initial injury Where the stenosis is not complete pulmonary suppuration supervenes and pneumonectomy is required

PENETRATING WOUNDS OF THORAX

Open penetrating wounds of the thorax fall into two general classes In one group the loss of thoracic wall substance is so extensive and usually the damage to the underlying lung is so great that salvage of the lung is impossible and reconstruction of an adequate thoracic cage on the injured side questionable The emergency management of each such case presents a unique problem and requires considerable improvisation

In general big defects are best sealed off with a large square of vaseline gauze many layers thick The square of gauze should overlap the wound margins by several inches on all sides and the multiple layers of gauze and vaseline should be approximately an inch thick This has some stability in its substance and can be taped to the chest with ordinary adhesive tape extending well beyond the margins of the gauze or applied by circumferential elastic bandages An air tight seal of the wound is obtained in this way yet serum and fluid collecting in the pleural space oozes out from under the margins providing fair drainage Definitive care often requires pneumonectomy and thoracoplasty to provide adequate coverage for the mediastinum

Less extensive defects may be handled the same way for emergency care and transported for definitive care quite satisfactorily Many of these can be closed primarily after careful debridement Extensively damaged underlying lung should be resected Areas of lung which expand well with intratracheal ventilation should be salvaged by suturing the air leaks which usually come from smaller torn bronchi Primary closure should be accomplished without the implantation of foreign material as these wounds are all contaminated and until the infection period is passed the implantation of foreign material is very hazardous If necessary a muscle flap may be shifted over the defect and skin flaps are always available for primary closure The areas from

which the skin flaps are moved can be covered later with split thickness grafts

The chest should be closed with suction by multiple catheters and lung expansion maintained Rapid obliteration of the pleural space aids in stabilization of the side Four to six months later during which time the chest wall may be stabilized by a fitted corset the defect may be repaired and made more rigid by implanting a thick Ivalon sponge pad sutured firmly to the edges of the rigid chest wall

Small sucking penetrating wounds result in the rapid development of a tension pneumothorax The air sucked in cannot get back out These are treated by intrapleural catheters which can stay ahead of the leak debridement of the wound, and closure If the wound is quite dirty simple debridement and the application of a vaseline gauze pad to stop the air leak is best

Closed penetrations where the wound of entry and if such the wound of exit are small enough that they promptly seal and do not allow exchange of air present few problems which have not already been discussed In juries to the heart and great vessels are frequent with this type of trauma and are discussed in that chapter

Closed penetrating wounds almost always result in pneumothorax and often in tension pneumothorax This represents their most serious immediate hazard It is easily controlled with catheters placed through an interspace and connected to suction equipment These same suction catheters if properly placed will evacuate any blood which has collected and allow accurate evaluation of the rate of bleeding Persistent hemorrhage requires open thoracotomy and ligation of the bleeding vessels

Infection in open injuries presents a problem which can be handled by adequate antibiotic therapy Most closed penetrations result in so little trauma to the soft tissue and underlying viscera that debridement need not be carried out Retained foreign bodies of an organic nature should be removed but metallic ones of a centimeter or less in all dimensions are probably best left alone

SUMMARY

Thoracic injuries cause severe disturbances of respiration and circulation Injuries to the heart and great vessels are frequent and are dealt with in a separate chapter but clinically they must be managed concomitantly with the injuries to the chest wall and pulmonary parenchyma Adequate respiration requires pulmonary ventilation pulmonary perfusion and systemic circulation The cardiologist bronchologist and thoracic surgeon must work together as a team to meet these problems

Tracheotomy is probably the most valuable single procedure for the re establishment of pulmonary ventilation It is rarely done too soon frequently delayed much too long We have come to use tracheotomy more and more and the house staff is admonished to promptly establish a tracheotomy in all severe cases

After pulmonary re-expansion by suction catheter removal of air and fluid from pleural spaces and clearing of the tracheobronchial secretions by aspiration the flail chest wall often will stabilize with quiet respiration If not positive pressure intratracheal oxygen will usually suffice Adequate ventilation will promptly clear pulmonary edema of traumatic origin unless severe left heart injury has raised left atrial pressure

Crushing injuries of the chest resulting in muscle spasm immobilization of the ribs, or in flail instability accompanied by abdominal or diaphragmatic injury will require prolonged artificial respiration This should be immediately established by para-oral intratracheal intubation or by cervical tracheotomy A cuffed tube may then be inserted into the trachea and artificial ventilation maintained by manual bag pressure using a standard anesthetic machine Within a few hours ventilation by uncuffed tracheotomy tube and large volume mechanical respiration should be arranged

Sucking wounds require emergency closure by thick occlusive dressings early debride

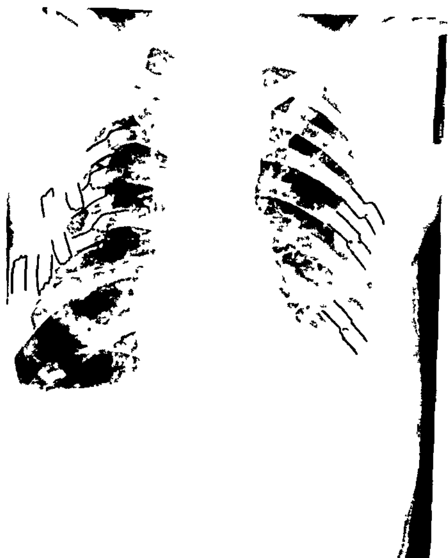


Fig 13 Roentgenograms of chest nine months after crushing injury (see Fig 4 acute injury) Fluoroscopy at this time revealed false motion persisting at offset rib fractures on the right side

ment and plastic reconstruction of the chest wall Hopelessly damaged lung should be excised on anatomical lines of lobe segment or subsegment Parenchymal tears suture readily and major bronchi and the trachea heal kindly after primary reconstruction by fine suture The rest of the problem is the same as in the closed injury

Patients failing to establish or maintain normal physiology despite adequate airway and re expansion of the lungs with replacement of blood volume require exploratory thoracotomy and the problem assessed by direct inspection Exploratory thoracotomy is as valid for diagnosis as exploratory laparotomy and should be as freely resorted to Many lives will be saved

Finally serious chest injury produces wide spread bony and soft tissue injury The pleural surfaces are torn and irritated by exudations and aggravated by continuous motion Respiration must go on and motion continues *with the production of unbearable pain* This demands relief with sedation Morphine in small doses of 1/6 grain or less reinforced with aspirin is probably the best drug Barbiturates are very dangerous for consciousness must not be obtunded

The essentially painful nature of the injury and its great prolongation by delayed union of ribs and cartilages and persistence of pleural reaction must be explained to patients and relatives and their cooperation gained by understanding. Later continuing discomfort must be cheerfully borne and breathing exercises practiced to regain thoracic motion. Brisk walking for gradually increasing distances up to three miles daily is probably the best of all breathing exercises.

Figure 13 illustrates a chest nine months after initial injury. Respiration was still painful with palpable costochondral offset and tenderness. Fluoroscopy showed motion of delayed union at malpositioned fractures posteriorly on the right. At 12 months golf was possible and pleasurable again for this self employed very successful business man.

It is well to remember the severity and persistence of thoracic pain after injury when prognosticating for patient, dependent, employer and compensator. Major thoracic injuries require a planned rehabilitation program just as other serious musculoskeletal injuries.

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CHAPTER 21

Air Contaminants

J Arthur Myers M D

In every part of the world the air is contaminated Pollens of plants and other material blown from the surface of the earth probably were in the air before humans appeared When man began to till the soil make implements from stone mine substances from the earth etc more foreign material entered the air With the industrial age such procedures as crushing and pulverizing increased the concentration of air contaminants There also appeared in the air of certain places poisonous substances such as arsenic lead and gases Moreover pathogenic micro organisms eliminated from the bodies of persons suffering from certain diseases often contaminate the air which people breathe Some air contaminants cause constitutional disease without resulting in damage to the lungs while others are capable of causing disease conditions in various parts of the respiratory tract

FUMES, GASES AND VAPORS

LEAD

Lead is often absorbed through the respiratory tract in the form of dust fumes or vapor Belknap studied 500 cases of lead absorption and concluded that even if complicated by actual disabling lead intoxication such as lead colic it does not reduce general resistance to upper respiratory infections or non specific pulmonary infections also that lead absorption does not impair general health as shown by

series also that lead absorption does not produce pulmonary fibrosis and that it does not predispose to or exaggerate pulmonary tuberculosis

CARBON MONOXIDE

This is a common cause of illness and death When inhaled the resulting disorder is of the nervous system and the actual lesions produced are due to the anoxemia and not to direct action of the carbon monoxide on the cells in the brain and heart Carbon monoxide readily unite with hemoglobin and thus reduces the capacity of the blood for carrying oxygen As this occurs an increased amount of air is breathed which in turn augments the absorption of carbon monoxide Carbon dioxide which is the normal stimulus for breathing decreases to the point where the victim stops breathing Along with this is loss of alkali If treatment is administered so as to prevent immediate death the patient may be comatose for as long as a few hours Inasmuch as pneumonia is responsible for a large percentage of those who die a few days after carbon monoxide poisoning it is important to prevent aspiration during the comatose state Carbon monoxide poisoning per se causes no permanent damage to the respiratory tract

WAR GASES*

A number of poisonous and irritating gases have been used in warfare During the first

* This subject is discussed primarily with reference to inhalation of gases and vapors For the effects of some of these substances on other parts of the body such as the skin and eyes the reader should consult the War Department's technical manual on "Treatment of Casualties from Chemical Agents"

World War mustard and phosgene were among the more poisonous. Page, who observed 6 000 gas cases, 2,800 of whom were serious, made the following statement: "We had rarely witnessed such suffering and distress as these patients manifested, with skin burned and discolored, eyes swollen shut, spasms of choking, vomiting and struggling for breath, with the lungs literally drowned by their own secretions they writhed in pain until they became unconscious from the want of oxygen."

During the Second World War, in addition to mustard and phosgene, a new group of war gases known as the nitrogen mustard was available. They act as vesicants or necrotizing irritants to all tissues with which they come in contact, including those of the respiratory tract. In persons affected by them the irritated larynx and trachea may be soothed by the inhalation of steam. Codeine sulfate helps to control the cough, and when edema is present oxygen should be administered. If there is an elevation of the body temperature during or after the second day, pneumonia should be strongly suspected and should be treated in the usual manner. With these new gases it was anticipated that, as is true of mustard and phosgene, most deaths would be due to respiratory involvement. When pulmonary edema appears the outlook is unfavorable, and bronchopneumonia is always a serious complication. Even in mild cases of tracheitis weeks may be required to control the cough.

HYDROGEN SULFIDE

Hydrogen sulfide causes irritation of the respiratory tract and may produce pulmonary edema and paralysis of the respiratory center. Exposure to high concentrations results in rapid panting breathing, early unconsciousness, cessation of respiration and convulsions. When high concentrations are inhaled, *mortality* is high.

NITROGEN DIOXIDE

Nitrogen dioxide fumes have been recorded *on a number of occasions to cause clinical* pneumonia and death among workmen in industry. Recently Grayson reported 2 cases and Lowry and Shuman 4 cases of nitrogen dioxide poisoning in silo fillers. One of Grayson's cases and 2 of Lowry and Shuman's cases died. One of Grayson's cases entered an unventilated silo and within 5 to 8 minutes was unconscious in a yellowish brown gas present *above the silage. He was rescued by his* nephew who was in the same gas only about 2 or 3 minutes. The first case died 29 hours after exposure from bronchopneumonia, although he received large doses of cortef during approximately the last 10 hours of life. The nephew, with less exposure, became seri*ously ill with evidence of chemical pneumonitis* involving all lobes. He received oxygen, broncho dilator drugs, penicillin and streptomycin. Within 48 hours he was much improved clinically, but 3 days later he developed fever when achromycin was substituted for penicillin and streptomycin. Within 24 hours he was afebrial and continued to complete recovery. Grayson reviewed the literature on silage gas poisoning, but the cases previously reported were thought to have been due to carbon dioxide inhalation or simple asphyxia. No gas analysis had previously been done.

The four cases described by Lowry and Shuman developed bronchiolitis fibrosa obliterans from silage fumes under essentially identical circumstances. Two of the cases died on the twenty seventh and thirtieth days after exposure. The two who recovered were given prednisone intramuscularly in doses of 10 mg three times daily.

Apparently the main danger from nitrogen dioxide exists during the first week to 10 days after a silo is filled. This information should be widely disseminated among persons who have silos that are not well ventilated to warn all persons against entering during this period.

NON TOXIC CONCENTRATION OF GASES IN INDUSTRY

The effects of long time exposure to non toxic concentrations of certain gases in industry, such as chlorine, sulphur dioxide, hydrofluoric acid, and *combinations of phosgene* with phosphorous oxychloride and phosphorous trichloride were made by Evans. Annual

roentgenographic inspections of the chest were made of men engaged in the manufacture of these gases Although their actual concentration in the air was not known, those who had worked for 4 to 10 or more years showed no trace of effects of the inhalations and the incidence of tuberculosis among them was no greater than in persons employed in other departments of the same plants Moreover, those persons who had so-called latent apical disease manifested no evidence of reactivation

Kehoe *et al* examined the chests of 95 persons employed in an electric refrigerator plant where *sulphur dioxide* was used No evidence of significant disease was found in any case Flury *et al* reported that workers in sulfide cellulose factories and on producer ovens remained relatively free from all infections of the respiratory tract including tuberculosis

Severe irritation of the respiratory tract including pneumonitis and pulmonary edema but causing no permanent damage may result from inhalation of excessive amounts of fumes, gases, etc of ammonia, cadmium, isoamyl acetate, methyl chloride and bromide, and vanadium Others such as acetone, acrolein, pentachlorol phenol and platinum may result in irritation but leave no permanent condition

Carbon tetrachloride (when heated phosgene is produced) results in irritation of the respiratory tract without permanent harm However, it may involve the central nervous system, the kidneys and the liver

When certain metals are volatilized the finely dispersed particulate matter formed may result in *metallic fume fever* The oxides of antimony, arsenic, cadmium, cobalt copper iron, lead, magnesium manganate, mercury, nickel, tin and zinc have been known to cause this condition Rohrs reported cases due to inhalation of zinc oxide Symptoms consist of throat irritation, tightness over the substernal area, malaise, headache, muscle cramps, chills, and fever The symptoms usually disappear within 6 to 24 hours without complications or residual

Tin, like iron oxide, may cause pulmonary nodulation without fibrosis It results in no disability

Insecticides have not been found to cause permanent damage to the respiratory tract, although in excessive amounts they may result in serious toxemia and even death

PULMONARY IRRITANTS AND TUBERCULOSIS

There is a general belief, and all too often among physicians, that pulmonary irritation, regardless of cause, increases susceptibility to certain infections, particularly tuberculosis The report of the surgeon general of the United States Army showed that among 70,552 American soldiers who were gassed during World War I, 173 cases of tuberculosis subsequently developed—a rate of 2 45 per 1,000—while the rate for all enlisted personnel overseas was 3 5 for 1918 and 4 3 for 1919 Later Price studied the experience of the armies of all the warring nations and reported that war gases had no influence upon susceptibility to tuberculosis Experiments on the effects of gassing tuberculous rabbits were conducted by Koontz, who was unable to find any change in the native susceptibility to this infection

Gardner believes that there is now sufficient evidence to indicate that the mere presence of inflammatory reaction in lung tissue does not alter native reaction to the tubercle bacillus by purely mechanical means and that there is no proof that local inflammation favors the implantation of tubercle bacilli nor does it necessarily bring about dissemination of infection from previously established foci of tubercle bacilli The significant factors responsible for the unfavorable course of a tuberculous process are more likely chemical in nature and only created by a limited number of specific irritants In the category of such irritants we now recognize free silica and tuberculin (not in doses used for testing)

INHALATION OF DUSTS (PNEUMOCONIOSIS)

Certain dusts in the air have long been regarded as harmful Hippocrates (460–380 B C) wrote about the difficult breathing of the metal diggers The elder Pliny referred

to refiners in the factory who enveloped their faces with loose bladder skin which enabled them to see without inhaling the fatal dust In 1556 Agricola said that mining is "a perilous occupation to pursue because the miners are sometimes killed by the pestilential air which they breathe Sometimes their lungs rot away Some mines are very dry and the constant dust enters the blood and lungs producing the difficulty of breathing the Greeks call asthma When the dust is corrosive it ulcerates the lungs and produces consumption Hence it is that in Carpathian Mountains there are women who have married seven husbands all of whom this dreadful disease has brought to an early grave"

In 1867 Zenker applied the name "pneumoconiosis" (derived from two Greek words meaning lung and dust) to include the conditions resulting from inhalation of dust of any kind Since dust is present in the air everywhere all adults have pneumoconiosis This varies in degree from those in whom the condition can be found only on postmortem examination to those in whom gross pathology can be detected during life

ORGANIC DUSTS

There is practically no evidence that inhalation of *organic dust* results in permanent damage to the lungs However there are some organic contaminants which cause irritation of the respiratory tract resulting in bronchitis pollinosis and asthma Indeed when an individual becomes sensitized to it almost any organic dust is capable of causing irritation of the respiratory tract A good example is pollens of various trees and plants which on sensitized tissues result in pollinosis See chapter 12 Similarly vegetable and grain dusts including that of wheat corn, oats and barley as well as animal emanations including hair fur and dander may cause asthma when inhaled by sensitized individuals

BYSSINOSIS

Byssinosis commonly known as cotton bronchitis occurs among workers in cotton rooms and card rooms The resulting condition is bronchitis or asthma

BAGASSOSIS

Bagassosis is a condition resulting from the dust of bagasse the waste of sugar cane after the sugar has been extracted This may result in an acute inflammatory pulmonary disease with extreme dyspnea and is probably due to a protein in the dust to which workmen become sensitized Numerous other dusts including that found in houses are capable of producing asthma

Bergman *et al* caused rabbits to breathe air containing *wood dust* in concentration of 10 million particles per cubic foot for eight hours a day five and one half days a week and found that it caused irritation of the respiratory tract

Persons may be sensitive to various *grains* used for human and animal food They have allergic symptoms when inhaling dusts of these grains from the final product or even while harvesting and sacking them Bacteria and fungi which accompany grains may cause irritations of the respiratory tract and asthma among persons sensitive to them

DUST AND SMOKE OF CITIES

Dust and smoke of cities cause a large annual loss due to waste of fuel resulting from imperfect combustion disfigurement of buildings requiring frequent cleaning and painting, spoiled merchandise in stores spoiling of clothes and injuries to vegetation In cities such as New York Chicago Boston and Baltimore as well as Pittsburgh and Salt Lake City it has been estimated that the annual economic loss from smoke amounts to from 10 to 30 dollars for every man woman and child In addition to this economic loss daylight and ultraviolet rays are absorbed by smoke in the air On smoky days in some cities as much as 50% of ultraviolet rays is prevented from reaching the surface of the earth

The measurement of air contaminants in

Cleveland from 1927 to 1929 showed that every month 119 tons of contamination from the air were deposited for each square mile in the downtown district This contamination consisted of dust which had been blown into the air from playgrounds parking lots unpaved streets and other areas uncovered by vegetation Handling of gravel and similar materials wrecking of buildings repairing and building of pavements iron from grinding processes wear of pavements rubber from the wear of tires and the heels of shoes and many other substances were thrown into the air by fast moving automobiles as well as the wind Tar dust resulting from the combustion of coal also constituted a considerable part of the contamination In addition to the material that could be collected there were large amounts of ammonia chlorine carbon monoxide nitric acid sulfuric acid and other substances which remained in the atmosphere and which were capable of having some effect on the human respiratory system

In Chicago in 1941 an average of 55 2 tons of dust fell from the air per square mile each month In one downtown area almost 135 tons fell each month

Inhalation of dust and smoke of cities results in a mild form of pneumoconiosis

Evidence has been assembled by Elstad which indicates that manganese in smoke is a serious offender He found that the production of manganese alloys from year to year since 1930 has followed a curve remarkably similar to those of the mortality and morbidity from pneumonia Haythorn and Meller made a study of 3 000 persons who had died in Pittsburgh hospital but found no tangible evidence to connect the deposits of pigment in the lungs to the high morbidity and mortality from pneumonia Although there is no good evidence that the ordinary dust and smoke of a city results in incapacitating disease the pneumoconiosis that it does produce the loss of ultraviolet rays in addition to the economic and aesthetic considerations are sufficient to enlist the support of the medical profession in its control

ATMOSPHERIC POLLUTION-SMOG

Air pollution has been defined as the presence in the atmosphere of substances not ordinarily found there or the presence of ordinary constituents of the air in greater than usual concentration "The natural behavior of the atmosphere coupled with the accidents of nature such as Vesuvius and Krakatoa and the industrial efforts of man have all conspired to force this public health issue upon us"

Atmospheric pollution may be extensive with marked reduction in visibility and the air is almost at a standstill without causing noticeable symptoms among people or damage to plants On the other hand with no more and even less visible evidence of air pollution there may be irritation of the eyes and damage to plants This is designated *smog* Probably concentration of certain polutants results in these damaging qualities which differentiate between smog and usual air pollution Photochemical reactions involving hydrocarbon oxides of nitrogen and sunshine are believed to result in smog

While elements composing smog exist in all large cities and some smaller ones it is only when lack of air currents sufficient to widely disperse them that they become especially noticeable Reference is often made to the city of Los Angeles where air is trapped Cool air that comes in from the sea cannot pass the mountains Moreover it cannot rise through the upper strata of warmer air Thus pollutants thrown into the air reach such concentration on occasions as to become harmful

Logan called attention to fog in the London area between January 3 and 6 1956 It was light on January 3 but became thick the next morning and persisted until the morning of January 6 The fog was thick enough to cause severe disruption of traffic, particularly on the evening of January 5 This condition was apparently responsible for approximately a thousand deaths in Greater London There had been severe fog in that area in November 1948 and December 1952 which apparently was responsible for many deaths After the

1952 fog, mortality records were studied during the previous 115 years to determine whether there had been any previous major increase in mortality associated with periods of severe fog Five previous incidents were discovered—December, 1873, January, 1880, February, 1882, December, 1891, and December, 1892 The apparent infrequency of such incidents throughout much of the 19th and the first half of the Twentieth Century and the fact that three incidents occurred from 1948 to 1956 suggested the possibility that either the atmospheric pollution associated with London fog has recently become more toxic, particularly to the very young, the infirm, and the elderly, or that there has been an increase in the number of persons especially vulnerable to its effects The 4,000 deaths that had been reported in December, 1952, together with the additional 1,000 in January, 1956, posed a serious problem

In October, 1948, prolonged heavy concentration of smog resulted in the death of 20 persons in Donora, Pennsylvania The exact cause was not known, but it was thought a combination or summation of action of at least two contaminants was responsible Sulphur dioxide and its oxidation product, together with particulate matter, were considered significant

These and other disasters such as those in the Meuse Valley, Belgium 1930, and Poza Rica, Mexico, 1950, were widely publicized so the disastrous effects of such episodes are well known

The annual loss from smog is tremendous It wilts plants, thus damaging gardens and other crops, soils and damages clothing, requires frequent cleaning of automobiles whole buildings, etc, and decreases visibility, thus resulting in accidents

The exact effect on the human body aside from irritating the eyes is not yet known, but there is evidence that it impairs efficiency

Apparently motor vehicles contribute more of the materials out of which smog evolves than anything else Industrial wastes are given second place and burning of rubbish, third Incomplete combustion is thought to be the important factor in all three of these sources of smog

Probably most of the materials from which smog evolves have long come from operating motors In some cities this problem has been markedly increased by converting public transportation systems from electrically operated equipment to that driven by gasoline and oil motors Roberts has pointed out that the exhaust from diesel powered equipment when operating efficiently does not contain carbon monoxide or aromatic hydrocarbons Toxic hydrocarbon is found in the exhaust of cold diesel engines and those otherwise inefficiently operating which animal experiments have shown to be carcinogenous

It has been estimated that not counting motors, about 20 per cent of the daily air pollution is derived from incinerators and various fuels for heating private dwellings

DUST STORMS

In 1935 Brown *et al* reported on the possible effects on health of dust storms which occurred in Kansas, Colorado, New Mexico, Texas and Oklahoma The predominating bacteria found in the dust were spore-forming soil types Molds were nearly as numerous as bacteria and some yeasts were found The silica content of the dust varied from 66 9 to 92 9% and the size of the silica particles varied from 2 to 770 microns, with a preponderance of the larger particles While there was no evidence that pathogenic organisms were carried by the dust the most severe epidemic of measles in the history of Kansas occurred at this time Acute respiratory infections were extremely prevalent throughout the State, and the dust was exceedingly irritating to respiratory mucous membranes Streptococcic sore throat was also prevalent

Smith et al found that season and dust control have a definite effect on coccidioidomycosis In one area where dust was controlled, the annual infection rate was 0 5 per 100 susceptible persons, while in two uncontrolled areas the rate was 20 to 25 per 100 Maximal incidence occurred in the arid dusty summer and autumn Grassing, paving roads and runways, and ultimately the use of highly refined oil on athletic areas were important dust con-

trol measures Indeed, they reduced infection rates from one-half to two-thirds

RADIATION

It has long been known that x-rays and other forms of radiation can cause great harm when improperly used Atom weapons in warfare are extremely destructive The atomic bomb, dropped over Hiroshima August 6, 1945, (estimated population 360,251) is reported to have left 78,150 dead, 13 983 missing, and 37, 425 injured Numerous deaths occurred later as direct or indirect results of the bombing Five hundred thirty-one civilian-owned animals, including horses cattle, swine, and pets were killed

The army animals which had just finished feeding at the time of the bombing consisted of 290 horses, 20 dogs, 160 swine, two cows 510 chickens and 50 ducks The bomb killed 205 of the horses, the 20 dogs, 95 of the swine both cows, 250 chickens, and all of the 50 ducks Destruction of animals decreased with distance of their location from the epicenter of the bomb In fact among those located beyond 2,000 meters 100% survived

It is such destruction that causes great fear in the minds of people of the air as a result of bomb testing Rumors pertaining to danger have been rife However nuclear energy has been so controlled by the Federal Government as to prevent any widespread injury to either atomic workers or to the citizenry Government releases show that the source of radiation danger is well controlled and far below the danger level *outside the testing* grounds

X-ray radiation in excessive amounts results in serious tissue damage However, dosage has been standardized well within limits of safety so that present diagnostic and therapeutic x-ray procedures are harmless After it was shown that x-ray radiation of small animals such as mice, fruit flies, as well as germinating seeds caused various mutations in succeeding generations, articles were written and widely read which predicted that any exposure whatsoever to x ray would result in terrible mutations in succeeding generations and would also reduce the life expectancy of recipients Dosage was given no consideration nor was attention called to the fact that small doses do not cause damage to the above mentioned animals and insects immediately or remotely through the generations Nevertheless, these predictions were so widely publicized that for a time many persons refused x-ray inspection as a part of routine or periodic examinations

The National Academy of Sciences on Radiation Hazard has pointed out that human gonads should receive no more than 10 roentgen units of radiation from birth to the age of 30 years An x-ray film of the chest annually over a 15-year period should use up only 0 07 from the allowable 10 units

Obviously, therefore, there is no evidence that harm comes to the individual or his descendants by judicious use of the x-ray in diagnosis, not only as a routine measure but as an annual periodic procedure over a long lifetime

INORGANIC DUSTS

There are a number of inorganic dusts which apparently are *inert* in the sense that they do not cause significant damage when *inhaled* and do not predispose to tuberculous or other infections Among them are calcium, iron, carborundum, aluminum and barium

Apparently the earliest extensive studies on pneumoconiosis were made among *coal* miners, and the name "anthracosis," first used by Stratton in 1838, applies to the condition which in its simple form consists of deposits of coal dust in the lungs and lymph nodes

Crystallized carbon known as *graphite* apparently is harmless in pure form, but it may contain as much as 10% silicon dioxide which may result in fibrosis if inhaled in sufficient amounts and over a long enough time

Calcium does not result in pulmonary fibrosis Roebber reported on the effects of *dolomite* dust (carbonate of calcium and mag-

nesium—much of the common white marble is dolomite) in the lead mines of Missouri. X ray inspections of the lungs of men who had been exposed to the maximum concentration of dolomite dust over periods up to 40 years revealed no unusual lung pathology which could be attributed to the dolomite dust.

Brumfiel examined 1,309 cement workers and concluded that cement dust is harmless to the human lungs.

Zenker in 1867 was the first to describe *iron* in the lungs, and he named the condition it produced "siderosis." Naeslund subjected guinea pigs to dusts from *iron ores* of five different types over a period of 14 months. Four months after the dust inhalations were discontinued, x ray inspection revealed no evidence of disease but postmortem examination showed pneumoconiosis. Gardner found that when animals inhaled the dust of iron for 2 years a slight amount of chronic inflammation developed about clumps of dust-filled phagocytes but the reaction was not progressive.

Doig *et al.* examined 16 *electric arc welders*, in 6 of whom x ray films revealed diffuse generalized nodulation throughout the lung fields; 3 others showed some nodular stippling and exaggerated markings. In the remainder slight stippling was seen in certain areas and the linear markings were abnormally prominent. They did not know the cause of these changes but thought they were not due to silicosis.

Enzer and Sander examined 26 electric arc welders, in 5 of whom nodular shadows were seen on chest roentgenograms which simulated a modified type of silicosis. In 5 others the trunk shadows were markedly exaggerated, the appearance simulating prenodular fibrosis of the type seen in older foundry molders. Silicosis to a degree to cast such shadows was eliminated through careful histories. The 5 men with the nodular shadows had worked inside tanks where fumes became dense. They had done more of this kind of work than any of the others. One of these men following an accident died from pneumonia and postmortem examination revealed fine black pigment shown to be iron by K Fe Cn stain, which was distributed throughout the lungs. There was complete absence of scarring or fibrous nodulation and there was no evidence of silicosis. The x ray changes were apparently produced by the focal accumulation of iron pigment. It was concluded that deposition of iron oxide in the lungs is responsible for the x ray appearance of nodulation in certain welders who have used bare metal electrodes over a number of years. They found that unless the work is confined, causing massive concentrations of particulate iron in the fumes, deposition to an appreciable degree does not seem to occur. They called attention to the striking similarity of the x ray film appearance due to the deposit of iron oxide with that due to silicotic nodulation. Functional impairment of the lungs with such iron deposits appears to be entirely lacking, both as to the development of clinical symptoms or susceptibility to complicating infections.

Groh inspected the chests of 86 arc welders who wore welding masks for protection from ultraviolet light. One reason for the studies was that several of these men were rejected for military service at an induction center because of x ray film findings. None of the entire group of 86 had any complaint until the films were made. None had lost weight, they had good appetites, were not subject to frequent colds and upper respiratory disease, and were living normal lives. Most of these men were young and had spent all of their working years welding with the same firm on confined jobs. They never had been exposed to appreciable amounts of silica dust. The silica content in the air of the shop where they worked was negligible; therefore silicosis was ruled out. Gardner *et al.* exposed guinea pigs to arc welding fumes two or three times a day for 1 year. Chemical pneumonia developed in 50% of the animals, but there was no evidence of fibrosis nor did the fumes have any effect on tuberculous animals.

Dusts of some substances may cause *proliferative changes* and other abnormalities when inhaled. Some known to belong to this category are silicon dioxide and asbestos.

SILICON DIOXIDE

Approximately 60% of the earth's crust is composed of siliceous material, 12% of which

is silicon dioxide. Therefore free silica (SiO_2), which is responsible for the development of silicosis, is present everywhere. Probably the first silica industrial hazards began when prehistoric man originated the trade of working stone into implements. Since the time of Hippocrates a number of references have been made to the health of persons working in dusty occupations. In 1860 Peacock and Traube isolated particulate matter from the lungs of miners and in 1871 Rovida was the first to use the word "silicosis" after he had recovered silica from human lungs by chemical analysis.

Silica enters human bodies through food, drink and air. It is constantly present in bones, skin, nails, connective tissue, blood and the lungs. Indeed it is eliminated in the urine of normal persons in the amount of approximately 1 mg per 100 cc of urine. That silica is a normal constituent of the animal body is maintained by Heffernan, who believes it strengthens tendons, scar tissue, etc.

When the lungs of adults dead from almost any disease are dried and pulverized, an average of 1.13 to 2.0 mg of silica per gm of dried tissue is found on chemical analysis. Larger amounts are found in the lungs of persons who have more exposure to silica. For example, McNally found 7.06, 9.75 and 26.0 mg per gm of dried lung tissue of a steel foundry worker, hard coal shoveler and a granite worker, respectively.

Sweany pointed out that chemical analysis of lung tissue gives only the total silica content, which may occur as free silica or in the combined form of some silicate. If silicates are present to any great extent a high value of silica will be obtained. If at the same time the amount of free silica is small there may be little or no fibrosis, since with one or two exceptions silicates apparently are inert substances.

The natural *defense mechanism* of the human body protects most persons against severe silicosis even when high concentrations of silica dust are inhaled. Many of the particles of ten microns or less in diameter and nearly all of the larger ones are eliminated before reaching the lungs. The first part of the defense mechanism consists of the vibrissae which filter much dust from inhaled air. Large numbers of dust particles that enter the nose and pharynx are lodged in secretions and are expelled in the usual manner.

The trachea and bronchi are lined with ciliated epithelium which directs dust lodged in the secretions in the direction of the pharynx where it is swallowed or expectorated. The terminal bronchioles are so small that they do not permit passage of particles more than ten microns in diameter.

SILICOSIS

PATHOGENESIS

Some of the particles of silica of 10 microns or less in diameter pass through the smallest bronchioles and are lodged in the air cells or alveoli. Soon thereafter phagocytes (dust cells) ingest them. Some of the phagocytes containing silica probably find their way into the bronchioles and are later expectorated or swallowed. Some migrate into lymph channels, a part of which are lodged in the lymphoid nodules while others pass through and are filtered out by intrapulmonary and tracheobronchial lymph nodes. As silica continues to accumulate, the reticular cells of the lymphoid tissue proliferate to such an extent that the lymph flow is retarded and particles of silica which are later brought in by the phagocytes are not so readily eliminated. The damming back of lymph results in dilatation of vessels, and inasmuch as the phagocytes cannot pass through in the usual way, many migrate through the walls of the lymph vessels where they deposit their silica content in the areolar tissue surrounding the blood vessels, bronchial ramifications, etc. The areolar cells multiply so as to produce considerable fibrous tissue around the lymphatic vessels so a thickening appears along which are interspersed the enlarged lymphoid nodules which may be likened to widely spaced beads. The

formations of fibrous tissue may increase and coalesce At postmortem examination Vorwald has found cavities which he designates anaemic type They develop within areas of massive fibrosis but show no evidence of causative organisms or cellular reactions These cavities are probably due to local deficiency in the blood supply although the toxic action of high concentrations of silica may play a part The decreased blood supply results in areas of local necrosis which because of autolysis ultimately liquify and evacuate

Various other conditions such as emphysema with pleural blebs abscess spontaneous pneumothorax pulmonary artery thrombosis hemorrhages extensive adhesive pleurisy pericarditis atelectasis and hard tumoral masses or hyalinized connective tissue are seen in some cases Hagen reported severe silicosis of the intrathoracic lymph nodes which resulted in disturbance at the bifurcation of the trachea with traction diverticula in the esophagus Perforation of one diverticulum led to pulmonary abscess formation bronchiectasis and generalized suppurative bronchitis

The exact mechanism through which silica results in fibrosis has been a subject of considerable controversy Gardner has suggested that it is silica in solution in the tissues which causes the changes since he found that the smaller the particles the more rapid and violent the reaction of the cells Others have contended that it is the hardness and sharpness of the particles of quartz which are responsible for fibrosis

DIAGNOSIS

Before the diagnosis of silicosis in any stage can be made there should be a *history* of exposure of 2 or more years (except in possible acute cases) to 10 million or more particles of dust of which 25 to 35% is free silica per cubic foot of air

In most persons who have silicosis no symptom is present and the condition never becomes detectable to any phase of the conventional physical examination or to x ray film inspection of the chest. However biopsy or necropsy study of lymph nodes (cervical and tracheobronchial) and pulmonary tissue reveals the presence of silica

After silicosis can be detected in the living body it may be classified as first second and third stages for descriptive purposes

Symptoms and abnormal physical signs are absent while the condition is in the *first stage* The x ray film reveals accentuation of linear markings along which one sees nodular shadows which represent the areas of greater deposits of fibrous tissue in and around the lymph nodules These present a somewhat beaded appearance *All the changes seen on the x ray film at this time may also be produced by other conditions* such as chronic bronchitis sarcoidosis bilateral bronchiectasis and passive congestion Gardner says "The increasing use of roentgenography has tended to confuse the picture by building up a pathology of shadows often without the essential confirmation of anatomic pathology" He also



both lungs A density is present in the apex of the right lung which was suspected of being tuberculous He was asymptomatic did not react to tuberculin and bacteriological findings were negative The shadows in the right apex were interpreted due to coalescence of silicotic nodules He was advised to continue regular work with protection against excessive concentrations of silica dust



Fig 2 Made from roentgenogram taken May 1944 of chest of man of 60 years For more than 25 years he had been a foundry moulder Extensive silicosis had been in evidence for several years but apparently had not increased His working capacity was not impaired except briefly when occasional small spontaneous pneumothorax occurred Without other interruption he completed his life s work and retired apparently in good health

says "The pathologist is not always impressed by the roentgenological diagnosis of linear fibrosis In the very advanced cases of so called linear exaggeration where many interlobular septa are appreciably thickened the x ray findings may be significant In those where half a dozen observers will differ as to whether the linear shadows are of unusual intensity there is every reason to disregard them

During the latter part of the *second stage* the first symptom namely shortness of breath may appear This usually is noticeable only on exertion and is by no means experienced by all cases

The nodules have increased in size through the deposit of fibrous tissue so they cast larger shadows on the x ray film (Fig 1) These nodules vary in size and some of them may be confluent so as to obscure partially or completely the increased linear markings At this time there is usually evidence of diffuse fibrosis

There are several other conditions such as fungus infections miliary tuberculosis tuberculous bronchopneumonia and carcinomatosis which cast shadows similar to those of silicosis in this stage

When silicosis is in the *third stage* there may be total absence of significant symptoms However some shortness of breath is usually experienced on exertion

When the pleura is involved chest pain occurs If there is sputum it is in small amount Gastro intestinal symptoms may occur reflexly resulting in loss of weigth and strength Symptoms which occur in this stage are often due to complicating infections

The areas of fibrous tissue produce large irregular shadows seen on fluoroscopic and x ray film inspection Pleural adhesions are often present resulting in distortion of the diaphragm and mediastinum Emphysema may exist and pleural blebs may be so large as to be mistaken for spontaneous pneumothoraces Spontaneous pneumothorax may also occur (Fig 2)

In order to diagnose silicosis in any stage the following must be present

(1) History of exposure for 2 or more (usually 15 or more) years to air containing more than 10 million particles of dust (of which 25 to 35% is free silica) per cubic foot The silica particles must be 10 microns or less in diameter and those of 5 microns or smaller are most significant

(2) Shadows on the x ray film which might be due to silicosis One must rule out the other conditions which cast similar shadows

(3) Symptoms must be present before one can diagnose disabling silicosis When disability occurs it is nearly always due to complications including emphysema cor pulmonale and tuberculosis

In the diagnosis of silicosis finding silica in supraclavicular including scalene lymph nodes or intercostal nodes or in the lung itself at biopsy or necropsy has no meaning with reference to clinical silicosis This is also true of finding nodules (silicotic) in lung tissue Such findings are not uncommon in persons working in silica dust but have no evidence of incapacitating silicosis

RAPIDLY DEVELOPING SILICOSIS

At one time the term "acute silicosis" was

applied to those cases who had been exposed to high concentrations of extremely fine pure silica dust and developed pulmonary conditions in a short time However further observation revealed that symptoms usually appear only after one to $1^1/_2$ years of exposure and the term was changed to rapidly developing silicosis" Fortunately such cases are practically non existent today

TREATMENT

There is no known treatment for silicosis If symptoms appear in the third stage such as shortness of breath slight cough and expectoration palliative measures may be administered and the individual should avoid exertion The human lungs have such large reserve capacity that even in extensive third stage silicosis there may be no shortness of breath When a diagnosis of silicosis is definitely established every effort should be made to prevent further inhalation of high concentrations of silica dust

PROGNOSIS

Gardner believes that one who has developed silicosis and is removed from the dust will have fibrosis develop progressively until all of the particles are encapsulated in nodules He does not believe that old nodules will continue to enlarge or that new ones form for an indefinite period Hayhurst says "Usually the lung effects of silica have about spent themselves by the end of two years after the last work exposure and thereafter unless the affliction is complicated by infection or emphysema (ballooning or blebbing) it remains practically stationary" Clement states that minimal simple silicosis is not a disease is not disabling and is not a cause of death Blaisdell has observed that a person can have a tremendously advanced silicotic process without physical disability

Judd concluded that when dust is controlled silicosis cases will not progress markedly unless infection supervenes and that uncomplicated silicosis is not a progressive disease without further dust exposure

Pendergrass says "We have passed through a period of hysteria and are now engaged in a healthy consideration of the fundamental problems concerned with the welfare of workers in dusty atmospheres" His careful studies over a period of 3 years of 329 men working in a pure silica hazard revealed that a large percentage of those who had worked for years and were exposed to high concentrations of finely divided silica dust do not show roentgen evidence of silicosis Nevertheless it is noteworthy that the total incidence of pulmonary abnormalities was 20% This figure closely approximates the general standard of 25% reported from most industries handling rock of high silica content The vast majority of abnormal chests showed slight lesions and few cases progressed from year to year When they did progress it was felt that superimposed infection was present Some of the lesions improved in appearance which would seem to justify the statement that individuals with silicosis need not necessarily have progressive disease Although the men worked in a pure silica exposure few had massive lesions and nodulations A number *of individuals with rather large lesions showed* no clinical finding or decreased capacity to do their jobs He observed that large lesions in the lungs may improve and individuals having silicosis with active infection should not be told that they are doomed They do improve and in some instances the lesions become quiescent so much so that they can begin to work again At one time it was believed that nearly every person with silicosis in the first or second stage was doomed that is the disease would continue to progress into the third stage However more extensive observations have resulted in a far better understanding of this condition

In 1939 Sander reported serial observations on 299 cases of silicosis selected from 3 377 foundry workers His observations had extended over $6^1/_4$ years Those with discrete nodulation in which no conglomeration of nodules had occurred were carrying on their regular work without undue effort or slowing up It was evident that even where there is considerable nodulation there apparently is sufficient respiratory reserve to prevent the marked disabilities associated with massive



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fibrosis and marked emphysema The 6 years of observation of these cases brought to light no case of visible progression of the silicotic fibrosis He believes that part of this apparent lack of progression undoubtedly can be attributed to the considerable reduction of the dust concentration in these foundries since his study began. It also adds further proof to the long-known fact that the lung changes occurring with mild to moderate silica exposure are extremely slow Sander concluded that it is safe to keep those with uncomplicated silicosis at their regular work under the controlled conditions of minimal dust exposure and adequate respiratory protection as well as under the medical control of periodic examination and absence of possibilities of acquiring tubercle bacilli at work.

[illegible] says "Recent experience indicates that workers with simple silicosis can continue to work in the foundry with little if any greater risk than in other occupations if excessive dust hazards are eliminated From the economic and social standpoint they are far better off there than unoccupied at home even if they receive compensation"

PREVENTION

There has been much speculation as to why one person develops demonstrable silicosis and another does not while apparently working under the same dust exposure Some students are of the opinion that there may exist individual susceptibility It is possible that one person's defense mechanism is more poorly developed or has been impaired through previous disease of the respiratory tract Sayers and Jones believe that respiratory infection is the chief predisposing and complicating factor in silicosis Infections anywhere in the respiratory tract whether acute or chronic are of the utmost importance since they affect the ability of the lung to rid itself of foreign material Anything t necessi
[illegible] deep breathing such as de
[illegible] and oxygen as encounter alti
[illegible] presence of abnormal igh
[illegible] quantities predispose to at
[illegible] is inhaled
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sible to determine who will develop silicosis under heavy dust exposure The fact is well established that in the majority there will be no evidence of this condition during life

It has been found that exposure to silica particles of ten microns or less in diameter with less than 5 million dust particles per cubic foot of air rarely results in significant silicosis Since these facts have been called to the attention of industries much has been done to eliminate the dangers For instance one large company with pure quartz dust exposure has reduced dust count from approximately 60 million per cubic foot in a part of one of its plants to less than 3 million the latter figure being far under the limit of safety

Urban states that when the granite industry in Vermont realized the hazards of breathing quantities of silica dust management installed over $100 000 worth of dust control equipment throughout all the cutting and finishing sheds of the Barre area He said studies indicated that little if any, roentgenological lung changes occur in workers exposed to concentrations of granite dust of less than 10 million particles per cubic foot and engineering studies have shown that this limit can be attained He pointed out that the mere installation of control apparatus is not sufficient to eliminate hazardous dust concentration proper maintenance and the cooperation of the workers using the equipment are equally essential Probably the most important single factor is good housekeeping that is the maintenance of clean work places free from accumulations of fine dust on walls rafters etc permits the size of expensive equipment necessary for suppressing dust to be kept at a minimum

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but the preventive aspects are now in fair order"

PROTECTIVE SUBSTANCES

For a long time it was suspected that certain substances inhibit the action of silica and thus diminish the liability of the development of silicosis These substances seem to modify delay or actually prevent the action of silica dust Hefferman is of the opinion that it is the clay in dust that protected the Derbyshire miners against silicosis Middleton suggested that when *clay* and silica are in the atmosphere the *clay* may agglutinate the silica so that the aggregates are too large to enter the lungs

Brumfiel observed that silicosis failed to develop from exposure to an atmosphere at first presumed to contain many times the theoretical safe concentration of silica particles in mixture with gypsum

Gardner reported that 15 to 20 years of exposure to high concentrations of *gypsum* and silica dust did not result in x ray or other evidence of silicosis among 100 men whom he carefully examined His experimental work showed that no pulmonary reaction occurred in animals after they had inhaled high concentrations of pure gypsum dust for years and that little change was observed in another group of animals after they had inhaled excessive amounts of equal parts of silica and gypsum dust over a period of 8 months whereas animals showed marked changes after inhaling pure silica dust over similar periods When atmospheric dust containing equal parts of gypsum and silica was allowed to settle the particles were found to be collected together in large aggregates

Gardner and Durkan said "The evidence indicates that particles of other minerals mixed with silica in the form of dust tend to inhibit the inhalation of such silica and to some extent neutralize its injurious effects upon the body" They believe that physical or chemical reactions between silica and inhibitor particles already inhaled into the lungs may prevent or retard the development of fibrosis

Sander believes the relatively high incidence of linear fibrosis in *iron* workers is possibly the effect of adulterant dusts in altering the reactions of the silica He says that undoubtedly the admixture of *carbon* and *iron* particles has had a material effect in preventing development of larger silicotic nodules among those he has observed The prominent trunk shadows are seen to be due to true fibrous tissue along the course of the lymphatic vessels

Denny *et al* observed that when rabbits inhaled quartz dust to which was added aluminum dust which composed less than 1% of the entire mixture they did not develop nodular fibrosis as did those which inhaled quartz dust alone Later they found that hydrated alumina reduced the toxicity of quartz in tissues by flocculation partially by absorbing silica from solution but primarily by covering the quartz particles with impermeable and an insoluble coating of gelatinous hydrated alumina Gardner conducted animal experiments which showed that aluminum and aluminum hydrate definitely inhibits fibrous reaction of tissues to quartz Moreover they prevent progression of silicotic lesions already established and actually cause retrogression in immature tissue responses In 1945 the Medical Research Council observed cases of pneumoconiosis in South Wales and found the most severe pulmonary reactions came from quartz but this substance was far less harmful in the presence of clean coal and did practically no harm when accompanied by shale

Apparently the development of silicosis depends upon the solubility of silica Therefore anything that coats silica particles such as iron oxide and alumina reduces their solubility Thus in places where it is impossible to reduce the silica content of the air to safe levels the addition of one of these protective substances may result in sufficient agglutination with silica particles so the aggregates become too large to pass through the fine bronchioles

PREVALENCE

Since silicon dioxide is so abundantly present everywhere it is obvious that in the strict sense of the word every adult has silicosis It is a condition which varies through a wide range from those persons who have only micro-

scopical silicotic nodules to those with extensive fibrosis in both lungs

Obviously the prevalence of silicosis which can be demonstrated in the living human body depends upon such factors as (1) the percentage of free silica in the material with which persons work (2) the fineness to which this material is reduced (3) the concentration of fine particles in the air breathed by workmen (4) the length of exposure (5) the presence of other substances in the dust which retard the action of silica on the lungs (6) past and present respiratory infections of workmen and (7) evidence required by physicians who make diagnoses

Reported cases of silicosis among *foundry workers* has varied considerably depending somewhat upon diagnostic criteria and protective measures that have been used Sander has long employed a most satisfactory classification He classifies those persons with slight exaggeration of the trunk shadows as *normal* He uses the term linear *fibrosis* for those with considerable accentuation of the trunk and linear shadows extending well out to the periphery of the lungs Those showing slight beading along the prominent trunk were also placed in the fibrosis rather than the silicosis group because such is a common finding in persons in the latter decades of life who never have been exposed to industrial dust In the *silicosis* classification he places only those in whom nodules can be seen in more or less *uniform distribution on sharp well taken roentgenograms* Moreover since other conditions are capable of causing nodular shadows on x ray films a history of adequate exposure to silica dust also was taken into consideration before a case was classified as having *silicosis* Using this classification he reported that among 8 377 foundry workers of all types 23% of the iron foundry workers had fibrosis and 5% had silicosis Among the steel workers 19% had fibrosis and 11% had silicosis whereas the brass and aluminum workers had rate of only 9% with fibrosis and 0 5% with licosis Indeed no aluminum worker was ound to have silicosis

In discussing why one should reasonably expect wide variations in silicosis incidence not only in different types of foundries but also in the individual foundries of the same type Sander points out that the larger the casting the harder the casting and the poorer the general housekeeping the higher will be the silicosis rate Among the nine steel foundries included in his study most of them did sand chipping and core removal with pneumatic hammers in the open cleaning room up to the time of his survey an operation which has caused more dissemination of fine silica dust in these foundries than any other process with the possible exception of leaky sand blast booths One of his largest steel foundries with 300 employees for instance had an incidence of 25% silicosis which was almost entirely confined to workers in the cleaning room and due to the combined effects of the core knockout and a badly leaking sand blast booth This foundry as well as several others now has substituted hydraulic core washing for the previous dry cleaning which practically has eliminated the hazard No new case of silicosis has developed in this plant in the past 6 years of periodic observation of these cleaning room employees However it was plants such as these which raised the total silicosis rate in steel foundries to 11% Similarly a few of his malleable and combined grey iron and malleable foundries specialized in large castings from which the complete removal of core sand blasting has been difficult to accomplish Except for two of these foundries the incidence of silicosis in all of the iron foundries would have been about 2% These dustier cleaning operations now have been isolated and casting cleaners equipped with respirators as a result of which no new case of silicosis has developed in 6 years of observation

The *granite* industry in the United States originally began in Vermont and has been carried on there for more than 130 years Russell et al showed by petrographic analyses of granite from the Barre Vermont district a silica content of 31 to 38% Drinker *et al* found the average dust count in the granite cutting trade of Barre ranged from approximately 60 million particles per cubic foot of air to less than 10 million depending upon the nature of the work done On the other hand the granite quarries men were exposed to dust counts in the air ranging from approximately

40 million to 150 million particles per cubic foot. Bloomfield *et al.* determined that in granite cutting 94% of the dust particles measured less than three microns.

Judd examined 850 granite workers in Vermont and found demonstrable silicosis in 18% of those who worked in air with a dust count of 30 to 60 million particles per cubic foot, in 5% among those who worked in 10 to 30 million, and 3% among those who worked in 10 to 20 million, and 2% among those who worked in air that contained less than 10 million particles per cubic foot. Of all these groups 12% were reported to have silicosis. Among *those who developed this condition* the average period of dust exposure was 24 years before it appeared.

The name *anthraco silicosis* applies to those cases in which anthracosis and silicosis co-exist. In reality this is only a modified form of silicosis. In such cases the silica is derived from the rock *adjacent* to the coal vein. In the transportation division of a coal mine excessive concentrations of silica dust in the air may result from sanding the tracks.

There must be a *history* of prolonged exposure to coal dust and excessive amounts of silica dust before one can suspect the existence of anthraco silicosis. Other factors in diagnosis and treatment do not differ from that described for simple silicosis. Likewise prognosis does not differ except that the development of silicosis apparently is retarded by the presence of coal dust.

COMPLICATIONS

Sweany states that *cardiac changes* are due to the burden thrown on the right side of the heart as the result of gradual compression and obliteration of the pulmonary vessels by the fibrous tissues surrounding them. He found that cardiac changes appear only in advanced stages of silicosis. Hayhurst says that even with the unusual burden placed upon the heart to pump blood through markedly sclerosed lungs in the case of advanced silicosis, cardiac enlargement and myocardial disease are not notable accompaniments of the condition. It is difficult to prove that even conglomerate silicosis is the primary cause of



Fig. 3. From roentgenogram taken [illegible] 1953 of chest of [illegible] tion [illegible] left lu[illegible] 1944 [illegible] in 195[illegible] sions in the left lung h[illegible]nged. He did not react to tuberculin and acid fast bacilli were not found. In 1954 necropsy revealed primary carcinoma of left lung with extensive metastasis. (From Myers, *Geriatrics*, February, 1956.)

cor pulmonale. Most cases occur in persons over 50 when essential disease of the cardiovascular system is common. However, the cardiac symptoms may be aggravated by massive fibrosis of the lungs.

McCann says: "The occurrence of *cor pulmonale* can be demonstrated only in extremely advanced cases of silicosis."

An unusual number of workers in cobalt mines in Schneeberg are reported to develop *pulmonary malignancy*. Rosposki found that during a period of $3^1/_2$ years over 8% of workers in such mines had cancer. The ore in these mines is radioactive. It contains nickel, bismuth, lead, tin, iron and zinc.

Kincaid *et al.* and Sunderman *et al.* found that nickel carbonyl in concentration of 20 to 40 parts per million caused chronic irritation of the respiratory tract with evidence of metaplastic changes in animals. However, such changes did not occur when the concentration was reduced to one part per million.

However, Vorwald *et al.* assembled evidence from 57,000 cases of pneumoconiosis and found primary carcinoma was reported in only three. Among 1,357 cases of silicosis studied in their own laboratory only one primary cancer was found, which is probably a lower incidence than is seen in routine postmortem examina

tions of the general population There is no evidence to indicate that *pulmonary* malignancies develop more frequently among silicotics than among other persons (Fig 3)

When an individual who works in a dusty occupation develops pneumonia the disease is likely to be attributed to inhalation of dust Pneumonia is a common disease among persons who are not exposed to silica dust, particularly those past middle life Therefore there is no way to determine that the older silicotics who have pneumonia would not have had it in the absence of silicosis Gardner found an extremely small percentage of workmen developed pneumonia in the West Virginia Tunnel where the silica content of the air was high

Judd observed only one case of pneumonia among granite cutters over a 2-year period The death rate from this disease over a longer period was between 3 and 4% which was less than that in the general population of the area

When *tuberculosis* complicates silicosis the condition is known as *silico tuberculosis* Animal investigations have shown that silicotic lungs are more susceptible to tuberculosis than normal lungs

In a study of tuberculosis infections in people dying from causes other than tuberculosis Sweany *et al* found that in none of the lesions resembling silicosis could there be found evidence of recent tuberculous activity The bacilli appear to remain in the old nodes and produce slight caseation and peripheral calcification but no cellular reaction While the bacilli may survive longer in the silicotic lesions there does not appear to be any more active tuberculosis in these cases than in those without silicosis In fact there was a much lower percentage of positive findings in the minimal silicotic types than in those showing progressive tuberculous lesions without silicosis

Most of the older literature has stressed tuberculosis as the outstanding complication as cause of death among silicotics even to as high as 75% of cases This figure originated from the South African gold mine studies in their natives with high tuberculosis rates With good diagnostic documentation Sander examined 4 035 foundry men of whom only 3% have silicosis with tuberculosis active or indeterminate Active uncomplicated tuberculosis was also found in 0 47%

Sander says One very surprising feature of these serial observations has been that our apparently uninfected silicotics do not seem to be acquiring tuberculosis as time goes on Not one of the 299 silicosis cases listed as not infected at their first examination has been seen to develop evidence of tuberculosis in the $6^1/_2$ years since this study began" Hayhurst states it is probable that tuberculosis among silicotics will prove to be an endemic question that is that the rates will be higher in centers or groups where tuberculosis is higher

Schepers emphasizes that inhaled quartz dust may enable the Bacillus Calmette Guerin (BCG) to provoke fatal pulmonary disease

Thus the alarm that was broadcast 20 or more years ago has been found unjustified in the vast majority of cases It was then stated that nearly everyone who develops silicosis even though it was found in the first stage was destined to have the condition progress and sooner or later must die from acute or chronic pulmonary infection such as pneumonia and tuberculosis or because of extensive fibrosis and emphysema cor pulmonale would claim the lives of others

It is now known that silicosis is not necessarily a progressive disease and that by no means do all persons who have it even in the third stage fall ill or die from silicosis or from complicating infections or of failure of the right ventricle Many men with silicosis live long normal lives with good working capacities

DISABILITY

Until recently there was no accurate method of determining the degree of disability among silicotic individuals Malingerers who feigned symptoms could not always be separated from persons who actually had disability With the advent of the x ray film evidence of silicosis could be detected in some cases long before symptoms and physical signs were present Unfortunately this resulted in much harm both to workmen and producers since it was

assumed that whenever shadows were found disabling silicosis existed

McCann and Kaltreider observed that when there is no evidence of infection pneumoconiosis may progress a long time without sufficient symptoms to interfere with the capacity to work provided the man is not made aware of the nature of the changes in his lungs However most workers in dusty trades have now been frightened by what they have heard and read about silicosis and few indeed are those who do not develop symptoms if they know that their roentgenograms are abnormal

Hurtado *et al* say "The interpretation of the roentgenograph of pulmonary fibrosis in terms of functional respiratory disability is one of the most difficult problems which confronts the physician in industrial medicine While the anatomical lesions of pulmonary fibrosis and their roentgenographic detection have been studied extensively the mechanisms responsible for the respiratory disability are inadequately understood"

Therefore it was exceedingly important that methods be devised by which the physician can determine with reasonable accuracy whether disability is present and if so to what degree McCann *et al* found that among individuals with slight to moderate increase in linear markings and hilum shadows the vital capacity and residual air were essentially the same as in normal individuals Among persons with nodular fibrosis there was little change However there was a general tendency to increase residual air and decrease vital capacity This was also true in persons with nodular fibrosis with beginning agglomeration of nodules Those who had dense areas of fibrosis and large emphysematous blebs showed a general lowering of vital capacity and increased residual air Thus simple nodular fibrosis is not accompanied by much change in capacity Abnormalities increase in frequency and extent as nodules coalesce and as compensatory emphysema develops

In recent years much study has been devoted to pulmonary function and books by such authors as Gaensler and Cordon present methods of determining pulmonary function with considerable accuracy (see Chapter 3)

SILICATES

Any salt of silicic acid is known as a silicate *Silicatosis* is defined as pulmonary disease caused by inhalation of dust of silicates Not all of the dusts of silicates used in industry have been carefully studied with reference to their effects on lungs However those which have been investigated with the exception of asbestos and possibly tremolite apparently do not cause more than mild pneumoconiosis which of itself is not incapacitating

SERICITE

Jones was strongly of the opinion that *sericite* results in serious pulmonary disease He showed that this mineral was contained in the lungs of those miners who had died from silicosis proving its presence by examination of histological sections with the polarizing microscope and by chemical analysis of the ash obtained from the lungs However his conclusions have not been confirmed and it seems probable the silica content of the dust was responsible for the condition he observed Indeed, Lemon and Higgins conducted thoroughgoing experimental studies but were unable to produce lesions even remotely resembling those of silicosis by injecting sericite

TALC

In 1942 Porro *et al* reported the finding of evidence of pneumoconiosis among workers in the *talc* industry They believe the dust responsible is the talc itself in the form of tremolite (calcium magnesium silicate) or soapstone (native hydrous magnesium silicate) or both since free silica or other dust in a high concentration was not found Tremolite talc is chemically much the same as asbestos The principle difference is in the physical rather than the chemical structure Talc fibers break and disintegrate more readily when rubbed be

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Sander says "One very surprising feature of these serial observations has been that our apparently uninfected silicotics do not seem to be acquiring tuberculosis as time goes on. Not one of the 299 silicosis cases listed as not infected at their first examination has been seen to develop evidence of tuberculosis in the 6½ years since this study began." Hayhurst states it is probable that tuberculosis among silicotics will prove to be an endemic question, that is, that the rates will be higher in centers or groups where tuberculosis is higher.

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tween the fingers than asbestos Symptoms of workmen consisted of dyspnea, cough, chest pain, and weakness *The authors state that* after disability occurs, recovery apparently is impossible On x-ray inspection, diffuse haziness and general nodulation were absent Microscopically, bands of fibrous tissue were found to surround the vessels and bronchi with thickening of the alveolar walls Gardner states that talc is extremely variable in *composition and while it sometimes occurs in* a relatively pure state, in other places it may be associated with significant quantities of free silica

ALUMINUM OXIDE

Lemon and Higgins found that when *aluminum oxide* was introduced, the lesions produced in animals were composed of aggregations of phagocytic alveolar histiocytes which gave *no evidence of multiplication or of trans* formation into fibroblast

BORO-SILICATE GLASS

When *boro-silicate glass* was used, the lesions showed some evidence of replacement by diffuse fibrosis in the stroma of the lungs *The earlier lesions were almost identical to* those resulting from aluminum oxide These findings suggested to the authors that the biological activity of uncombined silica is absent in the presence of these two substances and characteristic hyperplasia does not occur

MICA

Mica is a silicate mineral (aluminum silicate) Among persons who have worked in places for many years with a high concentration of fine dust, fibrosis has been found in the lungs *However, because of the complexity* of the different types of mica, there is still a question as to whether this substance itself *is responsible*

ASBESTOSIS

Asbestos is composed largely of magnesium silicate in *crystalline*, hydrated form and is always found with other minerals such as iron and usually contains about 2.6% free silicate *It has long* been known, in fact, attention was called to it by Pliny. A tablecloth made of it is said to have been owned by Charlemagne, *who had it cleansed by fire*

The large world producers of asbestos are Canada, Southern Rhodesia, Swaziland, South Africa, Cyprus, Russia, Australia and *the* United States The United States produces only about 6% of its domestic requirements from deposits in Vermont, Arizona, Georgia, North and South Carolina, Virginia, Maryland *and Montana During this century its use* has been greatly extended The rock-containing asbestos is *blasted in open quarries after which it is cracked and pulverized* Apparently, Murray, in 1900 made the first record of a case of asbestosis which was reported in 1906 Hoffman was the first person in this country to call attention to the magnitude of *the asbestosis problem In 1918 he stated* that 13 deaths from asbestosis had occurred among asbestos textile workers Pancoast *et al reported* 17 cases about the same time It was not until 1927 that the first complete description of the disease was presented by Cooke and the same year McDonald reported on its histology, showing that asbestosis bodies *originate from asbestos fibers in the lungs* In 1930 Lynch and Smith presented the findings of two autopsies on asbestos workers in which they discovered numerous asbestosis bodies They then detected such bodies in the sputum *of asbestos workers One year later they gave* the complete postmortem findings in a person who apparently had died from asbestosis

Sayers and Dreessen examined 541 men and women in the asbestos textile industry in North Carolina and observed the *most serious* forms of the disease in carders, spinners, weavers, twisters, willowers and pickers

Gardner *showed* that when particles and fibers of asbestos are inhaled, because of their size and shape *they apparently do not enter* the alveoli but lodge on the walls of terminal bronchioles where phagocytes ingest and carry *them into the substance of the adjacent walls* Here fibrosis results which may be sufficiently extensive to contract and *restrict the smooth* muscle Therefore, asbestos particles usually

do not reach the lymph channels. The lesions are diffuse rather than nodular. This is thought to be due to the way the asbestos particles differ in shape and character, thus preventing them from becoming grouped at focal points.

As the condition progresses, extensive fibrosis develops throughout the lungs. All of the pulmonary framework is involved. Walls of the alveoli acquire such thickness as to reduce the alveolar capacity. The visceral pleura also is definitely thickened, but there is evidence of little change in the hilum lymph nodes.

DIAGNOSIS

Before one can consider a diagnosis of asbestosis there must be a history of long continued exposure to asbestos dust. At first there is no *symptom*, but later shortness of breath may occur and become distressing. Cough may be severe and productive of tenacious sputum which at times is blood streaked. Often there is substernal pain and the individual becomes thin and weak.

One may occasionally observe clubbed fingers, and in extreme cases there is evidence of cyanosis. Limited movements of the chest wall on breathing become noticeable as the condition advances.

Early in the development of the condition *x-ray* film inspection reveals no abnormal shadow. Later there is exaggeration of linear markings at the bases. As the disease progresses, a ground glass or granular appearance is noted which in time obliterates linear markings. Usually there is no nodular or nodulo-conglomerate markings in asbestosis as one sees in silicosis. Sayers and Dreessen state that the apparent small amount of involvement of the lungs makes it difficult to evaluate the severity of the case from x-ray film inspection only and that asbestosis strikingly indicates the necessity for clinical study of each case before diagnosis can be made. The film of a person severely ill with asbestosis may have markings which appear insignificant alongside a film of a silicotic who is actually at work.

Sputum may reveal the presence of *asbestosis bodies* which are somewhat the shape of a dumbell and range in length from 20 to microns. The fact that they give a pru blue reaction to iron acids in identifying t *Sayers and Dreessen found such bodies i* sputum of 46.9% of persons whose cond was diagnosed as asbestosis and in 24.3 essentially normal persons who had bee posed to asbestos. Therefore the findin these bodies in the sputum does not n sarily indicate the presence of clinical a tosis.

TREATMENT

There is no specific treatment for asbes All that can be done is to remove the vidual from contaminated air as soon as condition is found.

PROGNOSIS

Prognosis depends on the extent of the dition when found, together with other plicating diseases which may develop.

COMPLICATIONS

There is no satisfactory evidence th excess of tuberculosis develops among w men in the asbestos industry. *Cancer of* lungs has been found in co-existence asbestosis but as yet there is no evid that it occurs with greater frequency an such persons than in those of the ger *population.* *Progressive cases of asbes* may develop extensive bronchiectasis or gorgement of the right heart with right h failure as a terminal event.

PREVENTION

Prevention consists entirely of protec workmen against the inhalation of asbe dust. There is considerable variation in time that elapses from the first exposur asbestos dust and the time evidence of fib is observed in different individuals. C have developed after only 18 months of posure. However in the majority a m longer period intervenes.

Sayers and Dreessen found that five m

particles per cubic foot of air is probably the threshold value for asbestos dust exposure With adequate exhaust ventilation near the source of the dust it is possible to reduce the exposure of a majority of asbestos textile workers to less than five million particles per cubic foot of air

BERYLLIOSIS

In 1933 Weber and Engelhardt described a pulmonary condition thought to be caused by *beryllium* Following this a number of reports emanated from Europe and the United States

Beryllium was first processed from ore in this country in 1931 and has since been extensively used Phosphor zinc beryllium silicate was first used in the neon sign industry in 1938 Since 1933 a large medical literature has appeared on toxic effects of beryllium

Van Ordstrand reported 450 cases and pointed out that in places where basic extraction of the ore is done the most common lesion is acute eczematous dermatitis Particles which enter abrasions in the skin may result in indolent ulcers and chronic granulomas develop after lacerations from broken fluorescent lamps containing beryllium oxide Such lesions are sarcoid like and are successfully removed by surgery

The upper and lower parts of the respiratory tract may be involved including pneumonitis in some cases That sensitivity of tissues to beryllium is responsible for the development of berylliosis has been suggested by a number of physicians Sander says *"There is strong implication of a sensitivity factor the nature of which is not yet understood"*

DIAGNOSIS

History of exposure is important However Sander states there is a complete lack of correlation of the degree of dust exposure and the degree of involvement Moreover the attack rate among exposed persons is lower than that of pneumoconiosis among those exposed to silica dust Chesner, Hardy and others have reported cases in persons who were not known to have worked in direct contact with beryllium but lived near beryllium plants

In the acute respiratory form non productive cough and progressive dyspnea usually are the first *symptoms* Other respiratory symptoms appear rapidly In chronic cases symptoms appear more slowly including cough shortness of breath anorexia and weight loss These symptoms often do not occur for some time after the disease is in evidence by x ray film inspection The lesions are interstitial granulomata and are evidenced as fine disseminated nodular infiltrations These may be found by the x ray shadows they cast for several years before symptoms appear

Presence of beryllium in tissues and in urine indicates exposure to beryllium but the amount found does not prove the diagnosis of berylliosis or severity of the disease if present Beryllium has been found in tissues and excreted for years after the individual has been removed from exposure without evidence of poisoning In diagnosis berylliosis needs to be differentiated from metastatic carcinoma fungus infection miliary tuberculosis sarcoidosis and silicosis

TREATMENT

Cortisone and ACTH are the only drugs yet reported to be somewhat helpful Sander calls attention to spontaneous remission which may occur in early lesions before there is evidence of fibrosis and emphysema and that remissions may be induced by pituitary adrenocorticotropic hormone or by adrenal cortical hormone therapy

PROGNOSIS

Van Ordstrand stated that about 1 in 8 persons dies from asphyxia approximately 1 month after onset of the condition in acute pneumonic cases while the remainder recover within about 4 months DeNardi *et al*

called attention to 468 persons treated between 1940 and 1952 for various types of beryllium intoxication of whom 431 were acute and 10 in the chronic pneumonitis group died Of the 37 who had chronic beryllium intoxication 8 died

Some human and experimental animal material suggested to Schepers that the granulomatous form of berylliosis is but one of the many histopathological manifestations of chronic pulmonary beryllium disease He said further that pulmonary cancer has been experimentally produced in rats on exposure to beryllium sulphate and beryllium phosphor and this poses the grave question whether human subjects exposed to beryllium compounds may not eventually develop similar neoplastic pulmonary changes

PREVENTION

Although the use of beryllium in the fluorescent light industry began in 1938 the first clinical case was not recognized until 1945 When it became known that berylliosis was originating from this source the use of beryllium phosphor was discontinued and a non poisonous substitute has been employed in the manufacture of fluorescent lights since 1949

However there is still a danger when destroying old lights which contain beryllium When they are to be destroyed they should be broken out of doors or in a waste container with great care to avoid breathing the dust or vapors When large numbers of lamps are to be broken respirators should be worn Broken lamps should not be placed in an incinerator but should be put in water or in an isolated place where people will not come in contact with them

Whenever beryllium is used workers should take advantage of all precautionary measures provided

DIATOMACEOUS EARTH

The largest and purest deposits of diatomaceous earth now known are on the Pacific coast of this continent Diatomite consists of microscopical unicellular or colonial algae the silicified skeletons of which form kieselguhr (loose or porous diatomite) The unicellular algae have a cell wall of silica so the skeletons persist after death The accumulations of these skeletons through the centuries constitute a considerable part of the beds of certain lakes and seashore areas and hence diatomaceous earth is an amorphous form of silicon dioxide

Diatomite is of two general types That found on the shores of the sea is known as marine and that on the floors of extinct inland lakes is fresh water diatomite

Diatomaceous earth has been used in various ways for many centuries in fact since the days of the Roman Empire However its extensive use in industry is rather recent

In 1932 Legge and Rosencrantz reported that 68 5% of a selected group of Mexican workers exposed to diatomaceous earths presented shadow casting lesions on x ray film Smart and Anderson (1952) observed that the majority of workers in the diatomaceous earth industry in California are exposed to at least three or four qualitatively different types of silica some of which appear to be quite toxic Differences in particle sizes were also observed They described the manufacturing processes involved in producing the desired useful products and presented their clinical experience from six Pacific Coast plants processing diatomaceous earth

These authors emphasized that the majority of persons employed in this industry had no chest abnormality observed on x ray film and that most of those with definite findings had worked in the plants from 15 to 25 years There was absence of focal discrete nodules and whorled patterns of collagenous fibers on histo-pathological examination as seen in silicosis

When present x ray changes were of two kinds those of pneumoconiosis of the linear type and those with confluent or massive lesions (Fig 4) Massive lesions were usually seen in the infraclavicular and mid zones of

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DIAGNOSIS

History of exposure is important However, Sander states there is a complete lack of correlation of the degree of dust exposure and the degree of involvement Moreover, the attack rate among exposed persons is lower than that of pneumoconiosis among those exposed to silica dust Chesner, Hardy and others have reported cases in persons who were not known to have worked in direct contact with beryllium but lived near beryllium plants

In the acute respiratory form, non productive cough and progressive dyspnea usually are the first *symptoms* Other respiratory symptoms appear rapidly In chronic cases, symptoms appear more slowly, including cough, shortness of breath, anorexia and weight loss These symptoms often do not occur for some time after the disease is in evidence by x ray film inspection The lesions are interstitial granulomata and are evidenced as fine disseminated nodular infiltrations These may be found by the x ray shadows they cast for several years before symptoms appear

Presence of beryllium in tissues and in urine indicates exposure to beryllium, but the amount found does not prove the diagnosis of beryllosis or severity of the disease if present Beryllium has been found in tissues and excreted for years after the individual has been removed from exposure without evidence of poisoning In diagnosis, berylliosis needs to be differentiated from metastatic carcinoma fungus infection, miliary tuberculosis, sarcoidosis and silicosis

TREATMENT

Cortisone and ACTH are the only drugs yet reported to be somewhat helpful Sander calls attention to spontaneous remission which may occur in early lesions before there is evidence of fibrosis and emphysema and that remissions may be induced by pituitary adrenocorticotropic hormone or by adrenal cortical hormone therapy

PROGNOSIS

Van Ordstrand stated that about 1 in 8 persons dies from asphyxia approximately a month after onset of the condition in acute pneumonic cases, while the remainder recover within about 4 months DeNardi *et al*

called attention to 468 persons treated between 1940 and 1952 for various types of beryllium intoxication of whom 431 were acute and 10 in the chronic pneumonitis group died Of the 37 who had chronic beryllium intoxication 8 died

Some human and experimental animal material suggested to Schepers that the granulomatous form of berylliosis is but one of the many histopathological manifestations of chronic pulmonary beryllium disease He said further that pulmonary cancer has been experimentally produced in rats on exposure to beryllium sulphate and beryllium phosphor and this poses the grave question whether human subjects exposed to beryllium compounds may not eventually develop similar neoplastic pulmonary changes

PREVENTION

Although the use of beryllium in the fluorescent light industry began in 1938 the first clinical case was not recognized until 1945 When it became known that berylliosis was originating from this source the use of beryllium phosphor was discontinued and a non poisonous substitute has been employed in the manufacture of fluorescent lights since 1949

However there is still a danger when destroying old lights which contain beryllium When they are to be destroyed they should be broken out of doors or in a waste container with great care to avoid breathing the dust or vapors When large numbers of lamps are to be broken respirators should be worn Broken lamps should not be placed in an incinerator but should be put in water or in an isolated place where people will not come in contact with them

Whenever beryllium is used workers should take advantage of all precautionary measures provided

DIATOMACEOUS EARTH

The largest and purest deposits of diatomaceous earth now known are on the Pacific coast of this continent Diatomite consists of microscopical unicellular or colonial algae the silicified skeletons of which form kieselguhr (loose or porous diatomite) The unicellular algae have a cell wall of silica so the skeletons persist after death The accumulations of these skeletons through the centuries constitute a considerable part of the beds of certain lakes and seashore areas and hence diatomaceous earth is an amorphous form of silicon dioxide

Diatomite is of two general types That found on the shores of the sea is known as marine and that on the floors of extinct inland lakes is fresh water diatomite

Diatomaceous earth has been used in various ways for many centuries in fact since the days of the Roman Empire However its extensive use in industry is rather recent.

In 1932 Legge and Rosencrantz reported that 68 5% of a selected group of Mexican workers exposed to diatomaceous earths presented shadow casting lesions on x ray film Smart and Anderson (1952) observed that the majority of workers in the diatomaceous earth industry in California are exposed to at least three or four qualitatively different types of silica some of which appear to be quite toxic Differences in particle sizes were also observed They described the manufacturing processes involved in producing the desired useful products and presented their clinical experience from six Pacific Coast plants processing diatomaceous earth

These authors emphasized that the majority of persons employed in this industry had no chest abnormality observed on x ray film and that most of those with definite findings had worked in the plants from 15 to 25 years There was absence of focal discrete nodules and whorled patterns of collagenous fibers on histo pathological examination as seen in silicosis

When present x ray changes were of two kinds those of pneumoconiosis of the linear type and those with confluent or massive lesions (Fig 4) Massive lesions were usually seen in the infraclavicular and mid zones of

particles per cubic foot of air is probably the threshold value for asbestos dust exposure With adequate exhaust ventilation near the source of the dust it is possible to reduce the exposure of a majority of asbestos textile workers to less than five million particles per cubic foot of air

BERYLLIOSIS

In 1933 Weber and Engelhardt described a pulmonary condition thought to be caused by *beryllium* Following this a number of reports emanated from Europe and the United States

Beryllium was first processed from ore in this country in 1931 and has since been extensively used Phosphor zinc beryllium silicate was first used in the neon sign industry in 1938 Since 1933 a large medical literature has appeared on toxic effects of beryllium

Van Ordstrand reported 450 cases and pointed out that in places where basic extraction of the ore is done the most common lesion is acute eczematous dermatitis Particles which enter abrasions in the skin may result in indolent ulcers and chronic granulomas develop after lacerations from broken fluorescent lamps containing beryllium oxide Such lesions are sarcoid like and are successfully removed by surgery

The upper and lower parts of the respiratory tract may be involved including pneumonitis in some cases That sensitivity of tissues to beryllium is responsible for the development of beryllosis has been suggested by a number of physicians Sander says "There is strong implication of a sensitivity factor the nature of which is not yet understood "

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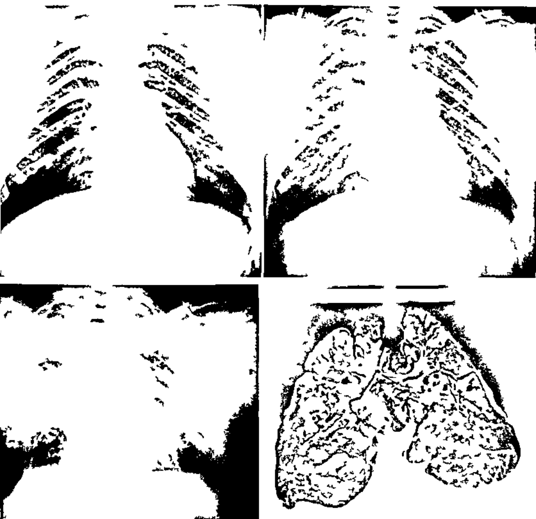


Fig 5 A White man born 1910 Employed 10 years as farm laborer Film taken at onset of employment $3\frac{1}{3}$ years in diatomaceous earth plant B Taken when transferred to outside work as gateman No further exposure C Shows massive coalescent fibrosis and bullous emphysema shortly before sudden death in 1945 Symptoms Severe dyspnea chest pain cough and expectora
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TREATMENT

Smart and Motley have found the use of intermittent positive pressure breathing with enriched oxygen mixtures and bronchodilator aerosols useful in combatting bronchospasm emphysema and arterial oxygen unsaturation A number of patients with severe cor pulmonale and heart failure have been successfully treated using these and other measures including antibiotics for intercurrent infections and aminophyllin to alleviate increased pulmonary vascular resistance Furthermore the

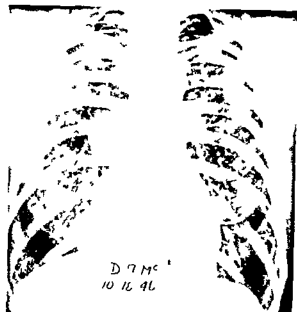


Fig 4 White man born 1892 Employed 15 years as machinist in non dusty industries then 17 years in diatomaceous earth industry Quit work 1946 because of exertional dyspnea Intra dermal tests Histoplasmin negative tuberculin and coccidioidin positive Serology coccidioides

ized reticulation with coalescent densities and associated bullous emphysema in upper lobes Autopsy confirmed coalescent lesions upper lobes and diffuse fibrosis of the basic type throughout

forma)

the lung sometimes accompanied by bullous emphysema in the bases and extreme apices Spontaneous pneumothorax was not unusual The diaphragm was markedly restricted in motion and although flattened it was definitely distorted

Clinically those persons who had evidence of linear fibrosis only usually did not present symptoms *Generally they had worked out* of doors and were exposed mainly to crude diatomaceous earth and natural powders However an occasional person working under these conditions over a long period progressed to the third stage of the disease Usually the extensive cases with no evidence of infection with bacteria or fungi had been exposed to calcined and flux calcined powders (Fig 5A B C and D)

In a few who later developed pulmonary tuberculosis tubercle bacilli were recovered with great difficulty prior to the appearance of cavitation Then the formerly benign disease progressed failing to respond to treatment except chemotherapy and resection

The main symptom in those with extensive lesions was dyspnea This sometimes appeared early in the course of the disease and was the chief cause of disability Fever and night sweat were absent except when complicated by tuberculosis In the confluent lesions the disease was often seen to progress for months and occasionally as long as 3 years after removal from the dust exposure In other cases progression apparently stopped when exposure was discontinued and often dyspnea decreased

The basic pathological pattern consisted of diffuse thickening of the pulmonary framework accentuated in the perivascular sheaths There was also increase in collagenous fibrils In some cases these apparently were the only changes due to dust In others focal coalescence of lesions was observed which varied from a centimeter in diameter to those involving the great part of a pulmonary lobe These coalescent areas were seen mainly in upper lobes and apices of lower lobes Extensive necrosis was observed and tracheobronchial lymph nodes were markedly enlarged

Based on pulmonary function studies Motley Smart and Valero said "Diatomite pneumoconiosis may produce a far advanced degree of pulmonary function impairment with a very severe degree of emphysema accompanied by a very marked decrease in the timed vital capacity and maximal breathing capacity a marked lowering of the arterial blood oxygen saturation and a marked decrease in *exercise oxygen uptake*"

No apparent correlation was noted in their study between the pulmonary function measurements and the chest roentgenologic appearance except when there were massive confluent lesions The evidence from the present study indicates that disability evaluation

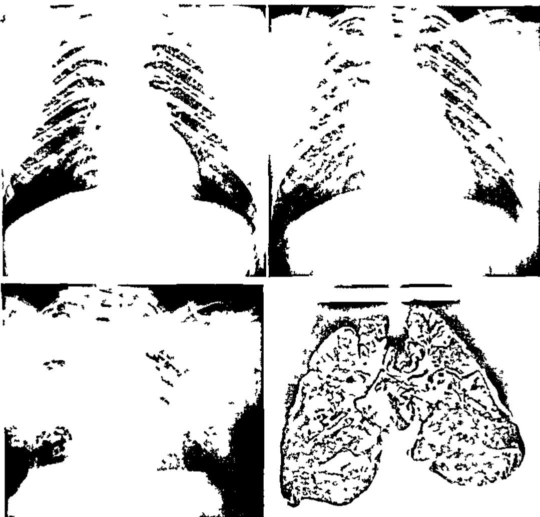


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early use of antituberculosis chemotherapy in those workers having positive tuberculin tests and progressive confluent lesions appears to halt further progression of the coalescent lesions

PROGNOSIS

Mild clinical cases apparently have good prognosis if the exposure is discontinued while some of those with extensive disease may develop incapacitating emphysema and cor pulmonale Smart and Anderson reported 20 workers who died from one cause or another in whom cor pulmonale contributed to death in 10 This also was a prominent feature in several others still living at the time of their report

PREVENTION

This consists of dust control measures wherever workmen are in contact with diatomaceous earth These measures are now in use, and it is possible that the extensive pathologic disease now found in a few workers is due to exposure before preventive methods were instituted

As in other dusty operations, industrial engineering measures are designed to control the dust at its source to provide adequate exhaust ventilation and the use of modern protective devices Periodic engineering surveys of the working areas including routine dust counts and periodic medical examinations of the workers including x ray films and basic pulmonary function studies are also essential for the protection of employees Motley Smart and Valero state that "Serial follow up studies of pulmonary function with the use of spirogram screening tests and residual air measurements appear to be the most reliable procedures to prevent the occurrence of the severely disabled condition observed in a few of the diatomite workers"

SHAVER'S DISEASE

In February 1942 Shaver examined a 33 year old man who had worked for 8 years in a plant producing abrasive material the main ingredient of which was bauxite The examination revealed spontaneous pneumothorax and a peculiar type of lung shadowing on x ray film Between 1942 and 1944 two additional cases from the plant whose x ray films showed similar shadowing came under his observation

In 1944 a chest x ray film inspection was conducted in the plants in which the abrasive was made Among the 1 913 employees only 344 were working in areas suspected of being responsible for the condition The disease was found to be well established in 23 early in 12 and doubtful in 13

In early cases symptoms were slight or absent but were sometimes severe in those with extensive involvement Sudden attacks of extreme breathlessness occurred in some cases and were found due to spontaneous pneumothorax These were observed in 9 of 23 cases with well established disease All cases complained of substernal discomfort and weakness Fatigue and sleeplessness were associated with advancing dyspnoea

In the original paper in 1947 by Shaver and Riddell the findings disclosed by four necropsies were described These showed patchy areas of pleural thickening and emphysematous blebs and bullae on pleural surfaces The lung substance was invaded by dense tissue of a non nodular fibrous character This was most dense in the central portion but more or less diffusely distributed The fibrous tissue was interspersed with areas showing marked emphysematous changes Microscopic examination revealed interstitial fibrosis involving the interalveolar septae

When Shaver made his original report he knew of no similar cases except that his cases resembled a condition reported by Goralewski and others in Germany from 1941 to 1943 These, however did not come to his attention until about 1945

In 1950 Riddell reported that there were then 30 cases of well established disease 29 early and 17 doubtful from four industrial

plants He pointed out that the fibrosis usually developed gradually but in certain instances it progressed with rapidity Spontaneous *pneumothorax often bilateral was a* special feature in the advanced stage and was present in each of the known fatal cases

Although the condition was not found prior to 1942 plants concerned had been in operation for at least 20 years Some years prior to *1942, a partial survey had been conducted in* one of the plants The films were not of the best quality, having been made by portable equipment Unfortunately however most of these films had been destroyed before the condition came to light However a remaining film of one of the fatal cases showed shadowing strongly suggestive of early disease At the time of the survey however this was ascribed to tuberculous infiltration

It is possible that earlier cases may have been erroneously diagnosed Since a review of the earlier death records in these plants showed a rather high rate from pneumonia and coronary thrombosis which in the absence of adequate documentation could have been due to spontaneous pneumothorax and other aspects of the disease

There was also the possibility that exposure in the plant was markedly increased during World War II when production increased about 10 times without a corresponding increase in working staff

ETIOLOGY

Riddell pointed out that the etiology of Shaver's disease had not been definitely determined by 1950

The abrasive manufactured in these four plants is corundum which occurs in several forms in nature It is an aluminum oxide of extreme hardness widely used as an abrasive Emerald topax sapphire and oriental ruby are forms of corundum

The material used in processing consists of a mixture of bauxite iron and coke Bauxite is a ferruginous aluminum hydroxide In this process the bauxite is first ground and intimately mixed with the other ingredients iron and coke This mixture is placed in large metal pots and by means of carbon electrodes it is fused at a temperature of 2,000° C Dense white fumes evolve from pots and escapes through openings in the roof of the furnace *room but a considerable amount* was present outside the furnaces where workers were stationed The fumes contain considerable quantities of alumina and silica and small quantities of other substances

Ashing of the lungs of the four cases on *which necropsies were reported by Shaver in* his original paper revealed silica ranging from 24 9 to 30 5% Alumina in the ash was not determined in one case but was 32% in one and 45 6% in the others

Pratt reported on experimental studies using two specimens of dust obtained from one of the plants where these cases had occurred The first sample collected from a furnace platform when injected intratracheally in guinea pigs resulted in no significant fibrosis within a year

The other specimen consisted of "fume from the stack of the furnace Electron photomicrographs revealed particles ranging from one half to a few hundredths of a micron in diameter with an occasional one larger than one micron Chemical analysis revealed a total of 32 3% of silicon dioxide and a total of 56% aluminum oxide Although accurate methods were not available for determining the amount of free silica there was some information which lead to the belief that a considerable quantity of the silica was uncombined There was also evidence that a fairly large proportion of the aluminum oxide was crystalline and therefore was not combined with silica

The stack fume was injected intratracheally into guinea pigs Twelve months later gross examination showed fibrous adhesions on the pleural surfaces and a pigmented scar running through an entire lobe of one lung *Microscopically diffuse fibrous tissue* was found in this scar closely resembling that seen *in human cases From all available evidence* it appeared that the stack fume was responsible for the disease Pratt believes that if the silica content of the fume is responsible its effect is greatly modified by the other components of the dust

PROGNOSIS

Prognosis apparently depends upon extent of disease when found. Seven of Shaver's cases had died by 1947, of whom all had spontaneous pneumothorax. There is suggestive evidence that acute pulmonary infections may be followed by rapid progression of the disease. Pulmonary tuberculosis apparently has not been a complicating factor. It is believed that incapacitating disease will not develop if persons on first manifestation of the condition are removed from further exposure.

From present knowledge Shaver believes that this condition can be at least partially *prevented* by:

1. Adequate diagnostic films.
2. Pre-employment x-ray film inspection of the chest to eliminate the medically unfit.
3. Immediate removal from furnace room exposure of any worker showing x-ray film changes suggestive of the disease.
4. Periodic x-ray film inspection of the chests of all exposed to fumes at intervals of 6 months or less as indicated.

Obviously, effort to prevent initial exposure to fumes is important.

PNEUMOCONIOSIS AND EMPHYSEMA

Emphysema is a complication which may occur in the presence of partial bronchial obstruction, pulmonary fibrosis, etc. In bituminous coal miners an excessive amount of coal dust may temporarily partially obstruct bronchial ramifications so as to result in localized areas of emphysema. Investigators in Wales believe that coal dust deposits around respiratory bronchioles where atrophy of smooth muscle occurs in bronchiolar walls resulting in excessive dilatation of bronchioles. This increases dead air space and ultimately interferes with exchange of gases with resulting exertional dyspnea.

However, Sander points out that most disabling emphysema, regardless of its cause, is primarily obstructive due at least in part to bronchospasm and that it can be improved symptomatically by bronchodilator aerosol inhalations and promotion of drainage of bronchial secretions. Gordon, Motley, Smart and Fowler have shown good ventilatory improvement with the use of both bronchodilation and *intermittent* positive pressure breathing. Fowler, however, found that bronchodilation alone gave as good results with his non-miner patients with obstruction as when intermittent positive pressure breathing also was used, suggesting that obstruction due to bronchospasm is the main cause of disturbed function in emphysema that is unrelated to dust exposure. Disabling emphysema associated with dust exposure also had been thought to be due primarily to airway obstruction.

Fletcher and Hugh Jones state that coal workers with simple pneumoconiosis (coal deposits plus focal emphysema) have relatively little disability and that most of the severe disability is found in miners with massive fibrosis. "Another clew is furnished in a recent paper by Wells which indicated that simple coal workers pneumoconiosis was not a major contributing factor in the 28 deaths due to failure of the right side of the heart out of 181 autopsies on miners with simple pneumoconiosis. On the other hand almost half of 136 with massive fibrosis died of cor pulmonale. In the present state of our knowledge it seems likely that focal emphysema per se is not a serious cause of impaired lung function. When an apparently real respiratory disability is found in a coal miner showing only simple pneumoconiosis by chest roentgenogram it appears that other causes for the dyspnea should be investigated including heart disease and diffuse obstructive emphysema due to other causes as well as the aging factor. Fletcher clearly states 'We do occasionally find men with simple pneumoconiosis who are seriously disabled but in such cases it is difficult to exclude the possibility that emphysema not of industrial origin is contributing to the disability!'"

Sander says: "More meticulous lung tissue studies as well as lung function studies correlated with histopathology are *necessary for* a better understanding of the various types of emphysema and their physiological differences.

Also lacking are reliable incidence figures on disabling obstructive emphysema in the population at various age levels. Until this information is available therapy of emphysema will stay more or less empirical and our understanding of emphysema and its relationship to dust exposure more or less clouded."

AIR-BORNE INFECTIONS

Wells has shown that during coughing and sneezing minute droplets containing microorganisms from infected surfaces may be ejected into the air. Most of these droplets are sufficiently small to evaporate before they can settle to the ground leaving suspended in the air minute residues known as *droplet nuclei*. These nuclei in which the microorganisms remain viable for considerable



Fig 6. Sneeze from subject with a bad cold. Note masses of viscid mucus which is less effectively atomized than saliva. The eyes are characteristically closed. Exposure $^1/_{30\,000}$ second. (From Turner, Jennison and Edgerton, *Am J Pub Health*, April 1941.)

periods may drift in air currents as would particles of cigarette smoke. Indeed they may actually remain in the air for days and be carried long distances from their sources. The air breathed commonly by persons congregated in rooms or other enclosed spaces can transfer organisms from one person to an other and deposit them upon the tissues of the respiratory tract. Turner, Jennison and Edgerton have made extensive studies of the origin of droplet and air-borne infections (Figs 6 and 7). Andrews stated that air-borne infections may be conveyed (1) in large droplet projectiles for short distances from the mouth or nose, (2) in droplet nuclei which may float in the air for long periods, and (3) on dust.

Buchbinder *et al* observed the number of *hemolytic streptococci* in air in several locations in New York City including schools, subway cars, theaters, streets and a park. More organisms were found in schools than in other locations but the subway was a close second. Torrey and Lake reported that the



Fig 7. A handkerchief or the hand held over the mouth in sneezing or coughing is an effective means of preventing the expulsion of potentially infective droplets into the air. Exposure $^1/_{30\,000}$ second. (From Turner, Jennison and Edgerton, *Am J Pub Health*, April 1941.)

prevalence of streptococci in the air of a large department store was influenced to a greater proportional degree by the number of colds among employees and customers than by the density of crowds. Wells *et al* are of the opinion that the number of streptococci characteristic of the nasal pharynx indicates

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the dissemination of respiratory disease The rationale of rendering air safe for human occupancy has been laid down in the laboratory and in suitable controlled human environments The means are ultraviolet irradiation dust suppressive measures and the use of germicidal vapors of hypochlorous acid and of propylene and triethylene glycol

Several methods have been devised to destroy microorganisms which have already been eliminated from patients and are present in the air on floors etc Lister used *carbolic acid sprays* to destroy micro organisms in the air within the range of childbirth and surgical operations There are several bactericidal mists effective against suspended organisms Andrews found a mist of sodium hypochlorite is cheap harmless in low concentrations almost odorless and a powerful deodorant Dust on floors can be prevented from rising by treating the surface once a month with spindle oil (crude liquid paraffin) Blankets can be prevented from dispersing their dust by soaking them in a 30% solution of liquid paraffin in white spirits Twort *et al* and others have presented evidence of the effectiveness of chemical sprays in destroying micro organisms in the air

Natural sunlight has long been known to have germicidal effects and therefore should be used as much as possible in places where persons are eliminating pathogenic micro organisms Andrews states that *ultraviolet light* is highly effective against organisms in droplet nuclei but much less so against organisms on dust Wells has shown that micro organisms can be destroyed in the air by ultraviolet rays at a rate far greater than that attainable by any type of mechanical ventilation By this method the spread of chicken pox and mumps has been prevented and the general incidence of respiratory infections as a whole has been markedly reduced

Wells and Lurie contaminated air with tubercle bacilli and introduced ultra violet light which killed 94% of the organisms Wells and Henle in experimental work on influenza were able to destroy 99% of the virus by introducing ultra violet light into the air Hart and others have shown that ultraviolet light reduces the number of organisms in the air of operating rooms

Miller *et al* devised a method of sterilizing small volumes of air by ultraviolet irradiation which may be of value in protecting persons working in laboratories where infectious aerosols or other air contaminants are discharged

Gilcreas and Read made a thorough going study of the effects of ultraviolet irradiation and triethylene glycol vapor as disinfecting agents in school rooms and school busses with the result that the number of air borne bacteria in these places was reduced but the incidence of respiratory and other communicable diseases was not affected among school children They pointed out that although the hours spent in school represent a large portion of a childs day he has numerous other contacts even in rural areas which play such an important role in the spread of infection that neither ultraviolet light nor glycol vapor can function effectively to reduce illness in a school situation

AIR CONDITIONING

Air conditioning is as old as the human race The cave man sought air as free as possible from undesirable factors for example he inhabited caves as protection from storms and heat of the sun Learning to produce fire was a long step in air conditioning and made it possible for man to inhabit many parts of the earth which otherwise would have been unsuited to him In due time he was able to leave the caves and build around him some protection from storms wind and the sun and when necessary to heat the air to a comfortable temperature

In the absence of food the human body may live for a few weeks in the absence of water for a few days whereas in the absence of air death ensues in a few minutes Our daily food and water requirements amount to a few pounds and a few quarts but of air approximately *12 000 quarts* are needed* In the

a hazard of respiratory infections and has a sanitary significance comparable with the presence of Escherichia coli in drinking water They estimated that several thousand nasal pharyngeal streptococci per sneeze are contributed to the atmosphere and state that the sneeze almost seems to be a provision of Nature for the survival of nasal pharyngeal parasites

Robertson s studies revealed that "The largest numbers of streptococci were dispersed by persons harboring these micro organisms in their noses and since such persons have been found to be the principal agents in the spread of streptococcal disease they are to be regarded as dangerous carriers Contamination of his surroundings bed clothes floor and air by this type of carrier was found to be due principally to blowing the nose sneezing and handling the nose and the mouth

Infection through the respiratory tract by air containing *tubercle bacilli* has been reported frequently and has become a routine procedure for experimentally infecting animals Augustine and Neufelt and many others have called attention to the contamination of the surroundings of patients with contagious tuberculosis Tubercle bacilli have been recovered from the dust of floors clothing bedding and in the air immediately after cough Duguid placed glass slides before the mouths of patients each of whom coughed six times From 20 patients studied 10 ejected tubercle bacilli Some of the droplets contained 40 000 bacilli Cultures from the throats of these patients revealed tubercle bacilli in 15 of the 20 whereas 10 presented tubercle bacilli in the anterior *mouth secretions* Lurie found that guinea pigs and rabbits acquired tuberculosis *when kept in the same room* but not in the same cage with tuberculous animals The incidence of this air borne infection increased with duration and intensity of exposure Sim and Flinn from a study of *tubercle bacilli* in the air concluded that these organisms fall out of the air rapidly and tend to stick wherever they are lodged so they are not stirred up into the *atmosphere*

Other pathogenic micro organisms such as *pneumococci* and *diphtheria bacilli* which attack the *respiratory tract* have been found in abundance in the air and in the dust of floors in hospitals where patients suffering *from these diseases are treated* Wells and Brown showed that the virus *of influenza* may remain suspended in the air for at least 30 minutes

Successful attempts have been *made to control air borne infections* Obviously the ideal method is to control them at their source that is in the body of the infected individual Delafield *et al* made a study of the effects of antiseptic snuffs containing proflavine penicillin and sulfathiazole and found that they temporarily reduced the number of organisms recoverable from the noses of staphylococcus carriers

Young *et al* reported the use of a *mouth wash* and *gargle* of watery acriflavine 1 in 5 000 twice daily for all patients admitted to wards with nose and throat conditions Prior to the use of acriflavine a great deal of post operative scarlet fever developed among their patients Indeed in a *single winter one of the* throat nose and ear wards had been closed 13 times because of this disease but during the 6 years following the introduction of acriflavine mouth wash they saw only five cases of postoperative scarlet fever

Andrews believes that adequate *spacing of patients* and *ventilation* are the most important counter measures whatever the route of dissemination of infections The spread by large droplets may be controlled (1) by isolation of infected persons (2) by screens between the heads of neighboring sleepers (3) by *masks of which one made of transparent* cellulose or acetate is comfortable effective and cheap though unsuitable for wearing at night Good ventilation is always important

West *et al* developed *contagious disease* technique for a tuberculosis service which markedly reduced the infection attack rate among student nurses This technique apparently prevents many tubercle bacilli from entering the air during coughing and sneezing and the consequent lodgement of *organisms* on floors bedding furniture etc

Mudd says "Respiratory disease is responsible for more than a third of the total number of person days lost to American industry by disability The air of enclosed spaces is at present the principal vehicle for

the dissemination of respiratory disease The rationale of rendering air safe for human occupancy has been laid down in the labora tory and in suitable controlled human en vironments The means are ultraviolet irradi ation dust suppressive measures and the use of germicidal vapors of hypochlorous acid and of propylene and triethylene glycol

Several methods have been devised to de stroy microorganisms which have already been eliminated from patients and are present in the air on floors etc Lister used *carbolic acid sprays* to destroy micro organisms in the air within the range of childbirth and surgi cal operations There are several bactericidal mists effective against suspended organisms Andrews found a mist of sodium hypochlorite is cheap harmless in low concentrations al most odorless and a powerful deodorant Dust on floors can be prevented from rising by treating the surface once a month with spindle oil (crude liquid paraffin) Blankets can be prevented from dispersing their dust by soak ing them in a 30% solution of liquid paraffin in white spirits Twort *et al* and others have presented evidence of the effectiveness of chemical sprays in destroying micro organisms in the air

Natural sunlight has long been known to have germicidal effects and therefore should be used as much as possible in places where persons are eliminating pathogenic micro organisms Andrews states that *ultraviolet light* is highly effective against organisms in droplet nuclei but much less so against or ganisms on dust Wells has shown that micro organisms can be destroyed in the air by ultra violet rays at a rate far greater than that at tainable by any type of mechanical ventilation By this method the spread of chicken pox and mumps has been prevented and the general incidence of respiratory infections as a whole has been markedly reduced

Wells and Lurie contaminated air with tubercle bacilli and introduced ultra violet light which killed 94% of the organisms Wells and Henle in experimental work on in fluenza were able to destroy 99% of the virus by introducing ultra violet light into the air Hart and others have shown that ultraviolet light reduces the number of organisms in the air of operating rooms

Miller *et al* devised a method of steriliz ing small volumes of air by ultraviolet irradi ation which may be of value in protecting persons working in laboratories where in fectious aerosols or other air contaminants are discharged

Gilcreas and Read made a thorough going study of the effects of ultraviolet irradiation and triethylene glycol vapor as disinfecting agents in school rooms and school busses with the result that the number of air borne bacteria in these places was reduced but the incidence of respiratory and other communicable dis eases was not affected among school children They pointed out that although the hours spent in school represent a large portion of a child s day he has numerous other con tacts even in rural areas which play such an important role in the spread of infection that neither ultraviolet light nor glycol vapor can function effectively to reduce illness in a school situation

AIR CONDITIONING

Air conditioning is as old as the human race The cave man sought air as free as possible from undesirable factors for example he in habited caves as protection from storms and heat of the sun Learning to produce fire was a long step in air conditioning and made it possible for man to inhabit many parts of the earth which otherwise would have been un suited to him In due time he was able to leave the caves and build around him some protection from storms wind and the sun and when necessary to heat the air to a com fortable temperature

In the absence of food the human body may live for a few weeks in the absence of water for a few days whereas in the absence of air death ensues in a few minutes Our daily food and water requirements amount to a few pounds and a few quarts but of air approxi mately *12 000 "quarts" are needed* In the

a hazard of respiratory infections and has a sanitary significance comparable with the presence of Escherichia coli in drinking water They estimated that several thousand nasal pharyngeal streptococci per sneeze are contributed to the atmosphere and state that the sneeze almost seems to be a provision of Nature for the survival of nasal pharyngeal parasites

Robertson s studies revealed that "The largest numbers of streptococci were dispersed by persons harboring these micro organisms in their noses and since such persons have been found to be the principal agents in the spread of streptococcal disease they are to be regarded as dangerous carriers Contamination of his surroundings bed clothes floor and air by this type of carrier was found to be due principally to blowing the nose sneezing and handling the nose and the mouth

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to a manufacturing company at Kosti Sudan They were jammed into a single room in an army barrack to await trial A little later 194 were found dead and 8 others were critically ill Cause of death was heat exhaustion and not changes in chemistry of air

Outside air is composed of approximately 79% nitrogen 20 96% oxygen and 04% carbon dioxide Other elements are present in small amounts The air that we exhale contains approximately 79% nitrogen 16 02% oxygen and 4 38% carbon dioxide Analyses have shown that in an ordinary house the carbon dioxide content of the air rarely exceeds four times that of outside air In order to have noticeable effect on the body it would have to be from 50 to 100 times as great that is a concentration of from 2 to 4% Even then there would be no serious effect Such concentration is never reached in homes or most buildings where people live and work In certain parts of breweries the carbon dioxide concentration in the air is from 0 5 to 2% but the employees do not experience ill effects The oxygen content normally found in outside air may be considerably reduced with no outward effect on the body for example in mines it is often maintained at 17% whereas at altitudes such as that of Pikes Peak it is approximately 13% With the latter concentration symptoms of mountain sickness may result but after a short time even they disappear At an altitude of approximately 1 mile such as that of some health resorts the air contains less oxygen than that of a badly crowded room at lower levels Therefore we need have no concern about the oxygen and carbon dioxide content of the air in most of our present buildings

The third reason for delay of refinements in air conditioning is the so called educational work of *fresh air faddists* To this day we are suffering from their teachings most of which are absurdities as they have never been based on fundamental principles yet often legitimate funds have been used to disseminate them

In 1909 Dr W A Evans Commissioner of Health of Chicago suggested the formation of a Ventilation Commission to study this subject experimentally and to make a start at least in securing some uniformity of ventilation laws and ventilation practices This suggestion resulted in the organization of the Chicago Commission on Ventilation in February 1910 The Commission published its report in 1914 following a large volume of careful scientific study which showed that immediate physical comfort is the standard of the human body and that this comfort is dependent upon the temperature and relative humidity of air more than other factors They found the comfort zone was between 64° with 55% relative humidity and 70° with 30% relative humidity

The New York Ventilation Commission appointed in 1913 also found that in most places where people live and work the temperature and relative humidity of air are far more important than its chemical constituents

Present day air conditioning includes control of temperature humidity air motion air distribution dust bacteria odors and toxic gases Equipment has been developed for conditioning air in respect to these factors

Where *heating* of air is necessary for comfort air conditioned spaces are provided with radiators to maintain the air at the desired temperature Outside air is heated to the proper degree and is then forced into the space in sufficient quantity for ventilating purposes only When indirect heating is employed the desired temperature is obtained by circulating air over heated surfaces as in furnaces located elsewhere By this method a large part of the warmed air is recirculated within the building and only enough outside air is admitted to ensure freshness and freedom from odor This method is more economical both from the standpoint of equipment and the use of fuel

Whenever it is advisable to *cool* air to insure comfort four ways have been used separately or in combination (1) Lowering the temperature (2) dehumidifying (3) evaporative cooling and (4) increasing air movement Reduction in temperature to a moderate degree combined with adequate dehumidification produces the best results for comfort In hot dry climates the most successful method consists of passing air through a water spray in which the air gives up a part of its heat and

course of selection of satisfactory food for man it was learned that certain plants were poisonous to all persons It was also learned that some food plants might become contaminated with disease-causing organisms, such as amebae, and that foods derived from animals often were contaminated with pathogenic micro organisms Therefore, it was necessary to condition foods by heating and cooking in order to destroy such disease-producing elements as well as to render them more palatable and digestible

When it was learned that drinking water may contain substances that are detrimental to health, including pathogenic micro-organisms, conditioning of such water was necessary Municipalities constructed filtration plants and other necessary equipment to render water safe for human consumption, as well as to give it a clear, wholesome appearance During the latter part of the nineteenth century and in the twentieth century to date billions of dollars have been spent throughout the world to ensure safe and wholesome food and water

Air, in which we are immersed and which is taken into our bodies in much larger volume than any other substance, was long neglected with reference to adequate conditioning There are three main causes for the *delay* in developing refinements in air conditioning The first is *mystery and superstition* Primitive man saw lightning, he heard thunder, he saw rain and snow descend, he heard wind whistle, and all were mysterious to him There is no clearer proof of ignorance and superstition concerning the air than the name "malaria," which is derived from "malo" meaning bad and "aria," meaning air This name was applied to a disease which was prevalent largely in areas where there was considerable stagnant water Odor from decaying animal and vegetable matter was noticeable in *the air the fog over the water was* visible and hence this name was applied to the disease decades before it was learned that *a mosquito bite was the real cause* Even tuberculosis and many other diseases such as those due to dietary deficiencies have been *attributed to the air*, which has also been looked to for a cure In fact, man almost overlooked the true factors responsible for improvement and recovery from tuberculosis in his great desire to give all the credit to "fresh air" Less than a century ago he even thought there were "immune" areas on the surface of the earth where people never contracted tuberculosis and that those who had it would get well if they moved to these areas

Another reason for the delay in refinements of air conditioning is that at first *only the chemistry of air* was considered, oxygen and carbon dioxide were discovered, and both were essential to life One must be taken into the body, and the other must be eliminated Therefore, the sole effect of air on the body was thought to be through its inhalation and exhalation Animal experiments were performed to prove the point For example, a mouse was placed in a small container with a candle The candle was lighted, and the container was sealed hermetically In a few minutes the candle went out, and the animal died The conclusion that so much oxygen had been used up that there was no longer enough to provide for combustion of the candle or the life of the animal, or that carbon dioxide had reached fatal concentration, was correct There is no question that oxygen is essential and that carbon dioxide must be eliminated, but usually people do not live and work in hermetically sealed containers Buildings in which people live and work have never been air-tight even with the windows and doors closed Therefore, while the animal experiment proved certain facts, practical ventilation should never have been built on these facts alone Yet on this basis, man sought to explain even tragedies For example, in 1756 when 146 prisoners were placed in a room 18 by 14 feet in the Black Hole of Calcutta, *only 23 were alive the next morning* Immediately the conclusion was that they used up the oxygen and there was a lethal excess of carbon dioxide There was adequate window space to supply an abundance of outside air The deaths were not caused by a lack of oxygen or an excess of carbon dioxide but by improper conditioning of the physical qualities of the air In February, 1955, approximately 200 years later, 285 cotton farmers were arrested for refusal to deliver their cotton

at the same time takes on humidity. Where cold water is available in sufficient quantity from deep wells, the air may be cooled by circulating over coils through which cold water is passing. Special air cooling devices are now available for a single room or for larger spaces.

HUMIDITY

Humidity of outside air when brought into a building is rarely satisfactory. When outside cold air is admitted and heated, it immediately expands. This markedly increases its capacity for water; therefore, unless moisture is supplied, the air becomes extremely dry. It takes moisture from furniture and from every other possible source, thus causing considerable damage. It even attacks the body, causing drying of the skin. Inhalation of such dry air has a harmful effect on the mucous membranes of the respiratory tract. Air with low humidity of from 5 to 10%, such as is frequently found in buildings during winter months, must be much warmer than properly humidified air in order to make the body feel comfortable; therefore, it is not uncommon to find in houses and apartments that the air is maintained at a temperature of from 80 to 90°F during winter months. When the temperature is reduced, the occupants feel chilly. However, when relative humidity is increased to 30 to 50%, the air is comfortable when the temperature is reduced to 68 or 70°F. Relative humidity of from 30 to 50% is regarded desirable for the most successful air conditioning.

In summer the humidity of outside air often is far too high. We speak of oppressive muggy days when we do not feel well and do not accomplish much. It is usually the high humidity plus the heat of the outside air that causes discomfort and inefficiency on those days. Such air should have a part of the humidity removed before it is admitted to buildings. Special dehumidifying devices have been developed for removing the excess moisture.

The amount of fresh air that must be introduced into a room for each person to provide adequate ventilation has been carefully studied. The smallest amount that will ensure freedom from body odors is 10 cubic feet per person per minute. The movement of air should not exceed 40 feet per minute in winter, but higher velocities are permissible in summer. Persons in rooms where the air circulates slowly have a lower incidence of acute respiratory infections than those in rooms where there is more rapid circulation.

Although equipment is now available for adequate conditioning of air, it sometimes is operated by persons with little or no understanding of the requirements of the human body. For example, in some places in summer excessively low temperatures and high velocities are used in air conditioned spaces in comparison with outdoor conditions. Moreover, the air is not properly dehumidified. Such extreme conditioning may result in discomfort and actually jeopardize the health of occupants of air conditioned places.

Outside air practically always contains some contamination. This varies from a small amount to that which markedly obstructs the sun's rays. One often thinks of air in the country as being clean and pure, yet there is practically no place on the earth's surface where the air is entirely free from particles of dust, and at some seasons it is literally loaded with pollen. During the spring of 1934 an extreme condition existed when the dust from the arid Dakotas, Montana, Kansas and Nebraska became so dense in the air that at approximately mid day it was necessary to use lights on automobiles. Even though windows and doors of buildings were tightly closed, there was enough leakage around them for much dust to enter. Hospitals were forced to discontinue surgery except in the most extreme emergencies. Despite the best methods available for keeping dust out of the air of operating rooms, it still offered considerable hazard to patients. Dust was carried by the winds to the eastern states and some extended out over the Atlantic Ocean. Thus the inhabitants of a large area were compelled to inhale much foreign material. While this was an unusual condition, dust storms frequently occur in some parts of the country. Volcanic dust has been found thousands of miles from

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Obviously in Los Angeles and other large densely populated areas where air is trapped some method of establishing adequate circulation of air may need to be devised In the meantime smog can be markedly reduced This can be by refraining from burning rubbish in open fires through systematic collection and safe disposal of combustible rubbish Exhaust fumes from motors in vehicles can be markedly reduced by keeping motors in proper operating condition by adjustment of carburetors gradual acceleration when driving keeping spark plugs clean replacement of worn piston rings etc Devices are now on trial intended to take out the fuel waste in or as it leaves exhaust pipes Controlling dust smoke etc in industrial plants is also helpful

Much may be done by appealing to the citizenry to discontinue the use of domestic incinerators to keep motors in good operating condition etc Daley Air Pollution Engineer city of Providence Rhode Island has demonstrated the rapidity with which progress can be made in controlling air pollution in a city by possessing the necessary information and procuring the cooperation of the entire citizenry

Tonney *et al* believe that our objective should be smoke eradication rather than smoke control and that the public health should be placed foremost and above all other considerations To accomplish eradication of smoke they advocate the central steam heating plant serving groups of buildings through underground connections over a radius of several miles Such plants are adapted to congested districts as they are not only more economical than large numbers of individual heating plants but also a large smoke-stack from such a plant replaces thousands of small ones Moreover from a limited number of large stacks there is greater possibility of controlling the smoke hazard Such central heating plants are already in operation in several cities

The use of gas both natural and artificial for heating is another way of solving the problem Gas combustion results in no ash or other solid particles While the products are gaseous in nature they do not obstruct ultra violet light Although heating by electricity has not been adequately developed to solve the problems because of its cost and the lack of potential electric energy it is possible that its use will be greatly extended Atomic energy may be a future solution

In some cities electrification of railroads and use of diesel engines within their limits has greatly reduced the smoke from locomotives The covering of vacant lots with vegetation such as shrubs and grass prevents a great deal of dust from being blown into the air The use of oil on unpaved streets and playgrounds as well as frequent washing of paved streets materially reduce the dust content of the air Methods are now available for reducing contamination from dust producing industries

Dry filters have been produced which remove most of the contamination from air before it enters buildings Air washers which have an effect similar to that of a rain storm on the atmosphere are valuable Electrical precipitation has also been found effective for the removal of ordinary dusts and bacteria Campaigns to destroy weeds before they pollenate in cities are helpful to those who suffer from pollenosis

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Tonney *et al* believe that our objective should be smoke eradication rather than smoke control and that the public health should be placed foremost and above all other considerations To accomplish eradication of smoke they advocate the central steam heating plant serving groups of buildings through underground connections over a radius of several miles Such plants are adapted to congested districts as they are not only more economical than large numbers of individual heating plants but also a large smoke stack from such a plant replaces thousands of small ones Moreover from a limited number of large stacks there is greater possibility of controlling the smoke hazard Such central heating plants are already in operation in several cities

The use of gas both natural and artificial for heating is another way of solving the problem Gas combustion results in no ash or other solid particles While the products are gaseous in nature they do not obstruct ultraviolet light Although heating by electricity has not been adequately developed to solve the problems because of its cost and the lack of potential electric energy it is possible that its use will be greatly extended Atomic energy may be a future solution

In some cities electrification of railroads and use of diesel engines within their limits has greatly reduced the smoke from locomotives The covering of vacant lots with vegetation such as shrubs and grass prevents a great deal of dust from being blown into the air The use of oil on unpaved streets and playgrounds as well as frequent washing of paved streets materially reduce the dust content of the air Methods are now available for reducing contamination from dust producing industries

Dry filters have been produced which remove most of the contamination from air before it enters buildings Air washers which have an effect similar to that of a rain storm on the atmosphere are valuable Electrical precipitation has also been found effective for the removal of ordinary dusts and bacteria Campaigns to destroy weeds before they pollenate in cities are helpful to those who suffer from pollenosis

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CONTROL OF SPECIAL DUST HAZARDS

Excessive amounts of dusts of free silica and asbestos occur only in certain industries

at the same time takes on humidity Where cold water is available in sufficient quantity from deep wells the air may be cooled by circulating over coils through which cold water is passing Special air cooling devices are now available for a single room or for larger spaces

HUMIDITY

Humidity of outside air when brought into a building is rarely satisfactory When outside cold air is admitted and heated it immediately expands This markedly increases its capacity for water therefore unless moisture is supplied the air becomes extremely dry It takes moisture from furniture and from every other possible source thus causing considerable damage It even attacks the body causing drying of the skin Inhalation of such dry air has a harmful effect on the mucous membranes of the respiratory tract Air with low humidity of from 5 to 10% such as is frequently found in buildings during winter months must be much warmer than properly humidified air in order to make the body feel comfortable therefore it is not uncommon to find in houses and apartments that the air is maintained at a temperature of from 80 to 90°F during winter months When the temperature is reduced the occupants feel chilly However when relative humidity is increased to 30 to 50% the air is comfortable when the temperature is reduced to 68 or 70°F Relative humidity of from 30 to 50% is regarded desirable for the most successful air conditioning

In summer the humidity of outside air often is far too high We speak of oppressive muggy days when we do not feel well and do not accomplish much It is usually the high humidity plus the heat of the outside air that causes discomfort and inefficiency on those days Such air should have a part of the humidity removed before it is admitted to buildings Special dehumidifying devices have been developed for removing the excess moisture

The amount of fresh air that must be introduced into a room for each person to provide adequate ventilation has been carefully studied The smallest amount that will ensure freedom from body odors is 10 cubic feet per person per minute The movement of air should not exceed 40 feet per minute in winter but higher velocities are permissible in summer Persons in rooms where the air circulates slowly have a lower incidence of acute respiratory infections than those in rooms where there is more rapid circulation

Although equipment is now available for adequate conditioning of air it sometimes is operated by persons with little or no understanding of the requirements of the human body For example in some places in summer excessively low temperatures and high velocities are used in air conditioned spaces in comparison with outdoor conditions Moreover the air is not properly dehumidified Such extreme conditioning may result in discomfort and actually jeopardize the health of occupants of air conditioned places

Outside air practically always contains some contamination This varies from a small amount to that which markedly obstructs the sun's rays One often thinks of air in the country as being clean and pure yet there is practically no place on the earth's surface where the air is entirely free from particles of dust and at some seasons it is literally loaded with pollen During the spring of 1934 an extreme condition existed when the dust from the arid Dakotas Montana Kansas and Nebraska became so dense in the air that at approximately mid day it was necessary to use lights on automobiles Even though windows and doors of buildings were tightly closed there was enough leakage around them for much dust to enter Hospitals were forced to discontinue surgery except in the most extreme emergencies Despite the best methods available for keeping dust out of the air of operating rooms it still offered considerable hazard to patients Dust was carried by the winds to the eastern states and some extended out over the Atlantic Ocean Thus the inhabitants of a large area were compelled to inhale much foreign material While this was an unusual condition dust storms frequently occur in some parts of the country Volcanic dust has been found thousands of miles from

its source Pollens are often carried hundreds of miles by winds

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Quartz is the most common form of free silica and occurs in flint, granite, sandstone, and other rocks. In rock drilling, the dust hazard is dependent largely upon the percentage of silica present.

The chief methods of controlling industrial dust hazards are (1) Substitution of non-dust producing or harmless substances, (2) isolation of dusty processes, (3) wetting dust at source, and (4) local exhaust ventilation applied at point of dust generation.

In some dusty occupations, such as removing cores from large foundry castings, sandblasting, handling of used storage battery plates and paint chipping, it is difficult to develop practical means of adequately controlling the dust generated. In such cases it is necessary to provide the worker with special respiratory protection devices. These usually consist of respirators or face pieces with filters, or masks or helmets using positive pressure. In either case difficulty has been experienced in convincing workers that they should be worn at all times while exposed to hazardous concentrations of dust.

In some industries dangerous fumes and gases are produced, such as those from lead and benzene. In all such places frequent analyses should be made to determine the concentration of these substances in the air and the necessary steps should be taken to keep them within safe limits. When this is impossible special masks should be used.

Atmosphere of Hospitals

Air conditioning of operating rooms is important for several reasons. First, there may be danger of explosions when ether and ethylene are mixed with air or oxygen in certain proportions. Static sparks in dry atmosphere are the most common cause of such explosions. The Committee on Anesthesia Accidents of the American Medical Association has recommended that the air of operating rooms contain 55% relative humidity and that special equipment be provided so that all apparatus, the operating table, the personnel and everything in the room is kept grounded at all times. The combination of oxygen with oil and grease may also result in explosions, so in winter months high humidity in the air of operating rooms is advantageous, not only from the standpoint of explosions, but also from preventing the loss of fluid from exposed viscera and the skin of the patient, as well as permitting lower room temperature.

There is good evidence that many of the infections which have occurred during operations were the result of air-borne micro-organisms. Hart and others have called attention to this hazard and have solved the problem in large part by flooding operating rooms with ultraviolet light.

Air conditioning has saved the lives of many infants born prematurely. Such infants actually freeze to death at room temperatures which are comfortable for adults because the premature infant's heat regulatory mechanism is not fully developed. Soon after the premature baby is born his body temperature begins to fall and death results unless some special means is used to condition the air. This conditioning has usually been brought about through hot water pads, heated beds, and incubators in which the temperature may be held at the desired degree, from 75 to 100°F. Not only must the necessary temperature be maintained within the incubator, but the proper humidity must be provided and the air kept in circulation. Complete air conditioning of entire hospitals is desirable.

MODERN DWELLING

Today the modern house is thought of in a different way than a few decades ago. Modifications in the plumbing and in the heating plant are made to condition the air, windows are immovable and so constructed that there is no leakage around them, the outside sleeping porch is obsolete, the ventilating system provides for the removal of contamination such as pollen, dust and other foreign materials, air is cooled or warmed to the desired temperature, moisture is decreased or increased as necessary.

Wiggs has described the numerous possibilities of conditioning for comfort which include a ceiling system which combines radiant heating and cooling and provides diffusers and ducts for supply of conditioned air.

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CHAPTER 22

Diseases of the Pleura

J Arthur Myers M D

The visceral or pulmonary pleura envelopes the lung and is closely attached to all of its surfaces At the lung hilum this serous membrane is reflected and becomes the inner lining of the entire chest wall—the parietal pleura Normally between these two layers there is only a capillary space containing just enough serous fluid to serve as a lubricant as the visceral pleura glides over the parietal layer during respiration

Before birth the lungs are solid and fill that part of the thoracic cavity not occupied by other structures When respiration begins outside air rushes through the trachea and bronchi into the lungs The diaphragm descends and an intrapulmonic pressure is established At the end of expiration in a new born child all air has been expelled from the lungs except that entrapped by collapse of the bronchi As the thorax enlarges relatively faster than the lungs the intrapulmonic pressure forces them to expand to fill all available space This through the elasticity of the lungs produces a negative pressure in the pleural space which is known as intrathoracic or intrapleural pressure Since the intrapulmonic pressure is usually approximately atmospheric the intrathoracic pressure is equal to one atmosphere plus the resistance offered to the intrapulmonic pressure by the elastic tissue of the lung and therefore the intrathoracic pressure is less than the atmospheric pressure and is designated negative pressure This varies with individuals and with the phase of respiration At the end of ordinary inspiration in an adult it may range from −1 50 to −7.50 mm of mercury while at the end of ordinary expiration it usually ranges from −3 00 to −4 50 mm of mercury

Negative intrathoracic pressure plays an im-portant role in the circulation of blo[od] lymph as well as in deglutition The [...] of the body is under atmospheric p[...] which affects the vessels such as the larg[...] of the abdomen the axilla and the ne[...] the same time the superior and inferi[...] cavae and the right atrium are under n[...] pressure within the chest On inspirati[...] negativity of the intrathoracic pressur[...] creased while the abdominal pressure b[...] more positive with the descent of t[he dia]phragm Thus the flow of blood in th[...] is facilitated by the atmospheric pressur[...] those of the abdomen axilla neck a[...] sucking action of those within the the[...] sulting from negative intrathoracic pr[...] The negative intrathoracic pressure ha[...] lating effect upon the esophagus with[...] thorax thus facilitating deglutition

Advantage is taken of intrathoracic [...] pleural) negative pressure in diagnosi[...] example when a lung is partially collaps[...] may obtain valuable information as to w[...] the pleural opening is decreasing in siz[...] factorily or is closed by introducing a [...] attached by rubber tubing to a ma[...] into the pleural space If a large volum[...] is still entering the space this pressure [...] that of the atmosphere whereas negativ[...] sure increases as the opening closes

When one introduces oxygen or air [...] presumably normal pleural space for dia[...] or therapeutic reasons it is important to [...] that the tip of the needle is in the [...] space This can be determined accurat[...] manometer readings

Pleural Fluid

With many diseases and conditions fl[...] various kinds accumulates in one or [...]



Fig 1 Fluid right pleural space Tubercle bacilli recovered

pleural spaces Normally the small amount of serous fluid in the space oozes from the visceral pleura This is absorbed nearly as fast as it forms so only a few cubic centimeters to lubricate the pleura are constantly present Any condition which causes more fluid to form or less to absorb may result in accumulation in the space

Accumulations of fluid usually occupy the most dependent part of the pleural space When individuals are examined in the upright position physically, by fluorscope or x ray film evidence of fluid is usually found at the base of the chest In addition to gravity there are other influences including capillary attraction between the parietal and visceral pleura viscosity and surface tension of the fluid and elasticity of the lung which determine shifting of pleural fluid These factors operating simultaneously account for the characteristic curved upper border of free thin fluid (Fig 1) sometimes extending to the apex when the individual is in the upright position Rigler has shown that when such individuals are placed in the Trendelenberg, the recumbent or lateral decubitus positions the fluid shifts to the most dependent part of the space This is especially true of thin fluids such as transudates and recently accumulated tuberculous effusion However, viscous pus with high surface tension moves more slowly if at all with change in body position

If air enters the pleural space only gravity controls fluid movements In the presence of air the upper border of fluid always assumes a horizontal level regardless of the position of the body (Fig 2)

Occasionally fluid accumulates along the medial surface of a lung and the physical signs and x-ray shadows simulate those of tumor Study of films made with the body in different postures may reveal the true situation

It is not unusual for fluid to become loculated or encapsulated As fluid recedes and the visceral and parietal layers of pleura come in contact and may become adherent so the remaining fluid is walled off Such encapsulations are most often seen in the posterior or lower part of the chest however, they are not uncommon in interlobar fissures Such loculations of fluid may be confused with pulmonary lesions

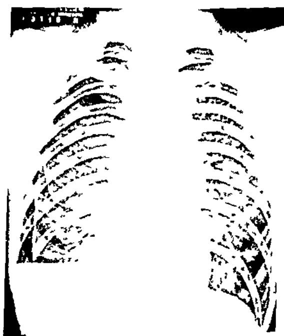


Fig 2 Fluid and air right pleural space, note horizontal fluid level

Chest Pain

Pain in the chest is a common symptom which may be caused by many conditions (see Chapter 2) The lung and visceral pleura are devoid of sensory pain nerve fibers except for a small area at the hilum Therefore pain in the chest does not originate from the lung or its pleural covering On the other hand the parietal pleura is richly supplied with pain nerve fibers and therefore pain results when it becomes inflamed through infection or is mechanically irritated Irritation of the diaphragmatic pleura may result in referred pain to the shoulder or to the upper or lower abdominal regions as seen in Figure 3 Such referred pain has often resulted in confusion in diagnosis particularly with an abdominal condition For example pneumonia involving the diaphragmatic pleura may result in severe pain over the right lower abdominal quadrant leading to the diagnosis of appendicitis Not infrequently following appendectomy with the pathologist report of a normal appendix pneumonia is discovered It was such occurrences in the past that emphasized the importance of careful examination including x ray film inspection of the chest prior to all surgical procedures Pleural pain is usually accentuated on respiration It ranges from a sense of discomfort to excruciating pain on inspiration

Most diseases and abnormal conditions which develop in the pleura are secondary to those which extend from adjacent organs or reach the pleura through the lymph or blood streams Practically all diseases that occur in the lungs chest wall and some originating in the abdomen are likely to involve the pleura

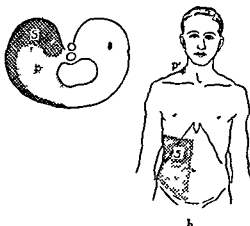


Fig 3 Results of stimulating the diaphragm with pressure P and S indicate regions stimulated P' over trapezius ridge is where pain is located [illegible] pressure pain spreads downward over the lower abdomen (Modified from Capps Arch Internal Med 8 722 1911 (From Rasmussen in Myers *The Chest and the Heart* Springfield Thomas 1946)

PLEURAL INFECTIONS

Infection may reach the chest so as to involve the pleura through lymph channels draining the head and neck passing through the supraclavicular nodes into the chest or from those in the chest wall passing through intercostal nodes Others from the abdomen pass through the diaphragm to the lymph nodes groups within the chest (Fig 4)

Miller has shown that the lymph immediately subjacent to the visceral pleura flows peripheralward into pleural channels and then to the hilum This facilitates spread of infection from immediately subpleural lesions Again lesions in lungs chest wall and abdomen may erode into the pleural space

TUBERCULOUS INFECTION

The tubercle bacillus is a common invader of the pleura The most usual source of bacilli is from subpleural lesions often parts of primary tuberculosis complexes The bacilli from these immediately subpleural lesions may reach the pleura by way of lymph channels or probably more often the lesions extend and actually discharge tubercle bacilli into the pleural space The pleura may also become involved from clinical pulmonary lesions of brief or long standings Lesions in the chest wall including ribs costal cartilages vertebrae supraclavicular and mediastinal lymph nodes may extend so as to involve the pleura

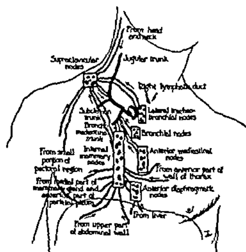


Fig 4. Diagrammatic sketch illustrating the lymphatic drainage from some of the deep portions of the thoracic wall. (From *The Normal Chest*, Baltimore, Williams and Wilkins Company.)

Fibrinous pleurisy begins to develop when tubercle bacilli reach the pleura which is sensitized to tuberculoprotein. Inflammation promptly ensues with large numbers of white blood cells assembled and fibrin deposits appear. Most often this occurs on the visceral pleura and hence no immediate pain is experienced. Through immediate contact involvement extends to the parietal pleura. Because of the sensory pain fibers in this layer of the pleura pain is likely to occur as the visceral pleura glides over the parietal layer. Often the two layers become adherent at the involved point and pain disappears. Organization of the fibrin results in fibrous tissue and the resulting adhesions permanently bind the two layers of pleura together. This is known as fibrinous dry pleurisy.

In other cases when the inflammatory process begins sero-fibrinous exudate forms and accumulates in the pleural space. This accumulation may be so small that it cannot be detected by physical examination or it may vary in amount reaching such volume as to markedly displace the mediastinum to the opposite side and extensively collapse the lung on the involved side. This condition is known as sero fibrinous tuberculous pleurisy often referred to as wet pleurisy or pleurisy with effusion.

Pleurisy with effusion is usually an allergic manifestation. Paterson could not produce immediate pleural effusion of demonstrable proportions by introducing virulent tubercle bacilli into pleural spaces of unsensitized animals. However, effusions occurred immediately when bacilli were placed in pleural spaces of those previously sensitized.

Lemon and Montgomery placed virulent bovine type of tubercle bacilli into pleural spaces of unsensitized rabbits. An extremely slight inflammatory reaction occurred with very small effusion which disappeared in three or four days. Within 15 to 30 days the animals became sensitized, as manifested by the tuberculin reaction. Then large effusions appeared and increased in amount until the animals died from generalized tuberculosis.

Pleurisy with effusion may occur soon after a high degree of allergy is established or at any subsequent time as long as allergy and living tubercle bacilli are present and free pleural space exists. A considerable number of our cases occurred in persons who were known to be nonreactors to tuberculin but who within a few weeks or months after exposure to cases of tuberculosis without adequate contagious disease technique were found to be reactors, pleurisy followed fairly promptly. In others pleurisy with effusion was the first manifestation that infection had occurred, as it appeared between the regular testing intervals. However, in all cases, when pleurisy with effusion was detected, the persons reacted characteristically to tuberculin.

Tuberculous pleurisy with effusion may make its first appearance many years after primary infection is acquired. For example, a physician who had a bout with primary tuberculosis as a medical student in 1892 later completed the medical course and conducted a general medical practice the remainder of his life. In later years x ray films revealed residuals of the old lesions in the form of calcific deposits. However, in 1944, at the age of 80 years, he experienced sudden excruciating pain over the right lower axilla and 2,000 cc of clear straw-colored fluid containing tubercle bacilli were aspirated. After a brief convalescence he resumed general practice, and he died from coronary disease at the age of 87 years.

Apparently tuberculous pleurisy with effusion occurs more frequently in young children who are invaded with tubercle bacilli than is generally believed If pain is present it may not be recognized by others and unless adequate examination is made the fluid absorbs without being diagnosed The youngest child in our group was 1 year old

There is considerable evidence that pleurisy with effusion occurs in adults much more frequently than is generally believed Many persons do not consult physicians unless pain and other symptoms are severe or persist In many cases symptoms are of short duration and fluid absorbs promptly and no examination is made Others are examined and the fluid is not found Still others are diagnosed as having pneumonia influenza neuralgia neuritis etc without adequate examination

Diagnosis

More cases of tuberculous pleurisy with effusion are seen by physicians in general practice than by others since the great majority of infected persons at any given time are apparently in good health The onset is usually acute and sudden and if medical consultation is sought, the family physician is the first to make the examination

Pleuritic pain which varies from mild ache to that which is excruciating usually is followed fairly promptly by fever Complete relief from pain may be experienced after hours or a few days owing to separation of the visceral and parietal pleurae by accumulation of fluid

The physician is hard pressed to make a diagnosis of tuberculosis in the absence of characteristic tuberculin reaction

In the beginning conventional physical examination usually is unrevealing except for splinting of the diaphragm and chest wall due to reflex protective mechanism Pleural friction rubs of dry pleural crackles are heard in some cases As fluid accumulates in sizable amount the percussion note becomes flat and egophony may be elicited immediately above the fluid

Fluoroscopic and x ray film inspections are of great value although they may be unrevealing for a few days or longer after the initial pain is experienced Rigler has shown that less than 300 cc of fluid in a pleural space is not revealed by ordinary fluoroscopic inspection or the usual postero anterior roentgenogram However in lateral decubitus position as little as 100 cc may be detected

Recovery of tubercle bacilli is the only incontrovertible finding in the diagnosis of tuberculous pleural effusion While clear straw colored fluid is suggestive in a tuberculin reactor it is not pathognomonic

Failure to recover tubercle bacilli may be due to such factors as (1) examining too small specimens (2) dilution of bacilli in a large volume of fluid (3) failure to use culture methods or innoculated animals In the past when tubercle bacilli were not recovered the condition was designated "idiopathic" and this was nearly always considered tuberculous

Stead and co-workers explored surgically 24 cases within a few months after acute effusion All 24 were presumed to have tuberculous pleurisy and were being so treated However 9 proved to be nontuberculous

Treatment

When fluid is allowed to remain in a pleural space fibrin is likely to deposit on both visceral and parietal surfaces to such extent as to cause them to appear thickened on x ray films with obliteration of costophrenic angles Occasionally extensive fibrothorax or calcification occurs markedly reducing pulmonary function Stead and co workers found fibrous peel more than 1 cm thick surrounding the lung in 13 of 15 persons explored surgically within a few months after acute effusion had been present

It is now believed that persons with tuberculous pleurisy with effusion should have the fluid removed and the pleural space kept as dry as possible thereafter that the usual anti tuberculosis drugs in the same combinations and dosage as used in pulmonary tuberculosis should be administered that strict bed rest should be prescribed for six months or longer if the condition warrants and that graduated exercise be employed leading to restoration of working capacity during the next six months Only time will tell whether antituberculosis drugs are effective enough to reduce the period

of bed rest and graduated exercise When cases are first seen after fluid has been present for weeks and there is evidence of fibrin deposits *decortication should be considered in* order to prevent permanent residuals

If present or future drugs prove effective in destroying all tubercle bacilli in the bodies of recent tuberculin converters it may be possible to cure tuberculosis including pleurisy with effusion if it appears soon after the tissues have become sensitized

Prognosis

Immediate prognosis in uncomplicated pleurisy with effusion is good Apparently remote prognosis differs little if at all from that *of persons who have no evidence of tuber*culosis except characteristic sensitivity to tuberculin Sizable groups of children and young adults have been followed over considerable periods after they became reactors to tuberculin and an appreciable number have been observed to develop clinical lesions in peripheral lymph nodes meninges lungs *bones joints and other organs whether or not* pleural effusion intervened In fact the majority of such cases did not have pleural effusion Among the students of medicine University of Minnesota graduating in the classes of 1930 to 1951 inclusive 963 became infected while in school or subsequently Pleurisy with effusion occurred in 20 of whom four later had clinical tuberculosis There were 25 of the 963 who developed clinical tuberculosis in four of whom pleural effusion had intervened

It is the underlying cause and not pleural *effusion* which determines remote prognosis This underlying cause is the foci of tubercle bacilli deposited in various parts of the body promptly after the initial invasion occurs All of them may remain silent during a person s lifetime On the other hand at any time after these foci are established one or more of them may provide bacilli for reinfection type of lesions Subpleural *ones* may cause pleural *effusion* those in the central nervous system may cause meningitis and so on with all acute and chronic clinical *lesions*

There is diversity of opinion regarding re*mote prognosis* This may be due in part to groups of patients reported *For example if* only persons with clinical tuberculosis who give histories of having had pleurisy with effusion some years before are considered conclusions can be *misleading In the areas from* which these persons originated there may have been several others who had undiagnosed effusions or were treated successfully with no *later tuberculous lesions*

Inclusion of demonstrable primary pulmonary infiltrates as clinical pulmonary disease can be deceiving Except for those who have chest wall lesions and the like, all persons with pleural effusion have antecedent *primary in*filtrates However relatively few are large enough have adequate consistency or are so *located as to be visualized on x ray films* From x ray shadows alone it is impossible to determine whether lesions are primary infiltrates or reinfection clinical disease This differentiation can be made only when periodic tuberculin testing has been done or by subsequent observation of the lesions Shadow casting primary infiltrates in any part of the lungs may be obscured *from view when fluid* is present and first be observed after it has absorbed or is aspirated Even then some such infiltrates are not visualized until they later have sufficient consistency to obstruct x rays In our experience primary infiltrates per se in children or adults rarely become significant clinically In a group of 236 cases of pleural effusion 55 presented pulmonary shadow casting lesions while fluid was present or soon after which proved to be primary infiltrates None subsequently became clinical

It is not unusual for interlobar fluid or that loculated anteriorly or posteriorly *to be mis*taken for pulmonary lesions from x ray shadows *This also applies to fibrin deposits* with or without fibrosis

Among 236 cases with 4620 person years of follow up 23 (9 7%) developed clinical tuberculosis In 10 the lesions were *in extrathoracic* organs and in 13 they were in the lungs

Prevention

Until recently prevention of tuberculous pleurisy with effusion was entirely dependent upon avoidance of initial invasion with tuber

cle bacilli Once the person was infected he was a potential case of pleurisy with effusion This applied to all clinical forms of tuberculosis Evidence is being adduced which strongly suggests that prompt antimicrobial drug treatment for recent converters may prevent meningitis If these drugs will prevent central nervous system lesions and those adjacent to blood and large lymphatic vessels from eroding into brain ventricles subarachnoid space and blood stream it seems possible that they may also prevent subpleural lesions from involving the pleura and causing pleurisy with effusion This has not been determined

RHEUMATIC FEVER

Sero fibrinous pleurisy with effusion occurs with some frequency in rheumatic diseases In fact it is believed that in the neighborhood of 2 or 3% of all such cases are due to this condition It is often immediately preceded by rheumatic pericarditis or pneumonitis

When pleurisy with effusion is first found a history of attacks of rheumatic fever and present other findings of recurrence are important in diagnosis In most cases the individual is seriously ill not only because of the pleurisy but also from the involvement of the other organs Occasionally pleurisy with effusion is found with less marked symptoms The condition has become subacute but there is nearly always a history of one or more rheumatic fever episodes or a rheumatic heart condition is present

Rheumatic pleural fluid is usually sterile However this does not rule out tuberculosis in differential diagnosis inasmuch as laboratory procedures fail to recover tubercle bacilli in many cases later proved to be tuberculous The occurrence of erythema nodosum just before or during the pleural attack is not helpful because this occurs both in rheumatic fever and tuberculosis The pleural exudate in rheumatic fever is more likely to be sanguinous than in tuberculosis

Treatment

Treatment of rheumatic pleurisy with effusion is that of the general disease plus palliative procedures referable to the pleurisy Sedatives may be administered freely to insure relaxation and sleep and to aid the patient in accepting bed rest Fluid should be aspirated as often as necessary to keep the pleural space as dry as possible This not only avoids accumulation which might result in cyanosis and dyspnea but also prevents fibrin peel from depositing on the pleura which might later require decortication

Prognosis is that of rheumatic fever itself

OTHER INFECTIONS

There are numerous other infections which result in pleurisy with effusion which are less commonly seen In fact practically every disease that causes pneumonitis may result in pleurisy with effusion

Brucellosis

An occasional person with brucellosis may have pleurisy with effusion There is nothing characteristic about the appearance of the fluid and Brucella may or may not be recovered from fluid cultures In the United States the majority of cases of brucellosis occur among persons in occupations or professions in contact with cattle and their products particularly veterinarians owners of cattle including members of their families and employees those who work in slaughter houses and butchers in any capacity Therefore the individual's occupation may provide a lead in diagnosis

In organisms not recovered from pleural fluid they may be sought in blood bone marrow and urine The blood agglutination test is dependable

Treatment consists of bed rest and sedatives as indicated Fluid should be aspirated and the pleural space kept as dry as possible Streptomycin or dihydrostreptomycin 0 5 gm intramuscularly twice daily and 0 5 gm aureomycin four times daily for 3 weeks has yielded best results to date

Prognosis is good if treatment is started early

Tularemic Pneumonia

Tularemic pneumonia may be accompanied by pleural effusion History of recent contact with wild animals or an ulcer on the surface of

of bed rest and graduated exercise When cases are first seen after fluid has been present for weeks and there is evidence of fibrin deposits, decortication should be considered in order to prevent permanent residuals

If present or future drugs prove effective in destroying all tubercle bacilli in the bodies of recent tuberculin converters it may be possible to cure tuberculosis, *including pleurisy with* effusion, if it appears soon after the tissues have become sensitized

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Immediate prognosis in uncomplicated pleurisy with effusion is good Apparently remote prognosis differs little if at all from that of persons who have no evidence of tuberculosis except characteristic sensitivity to tuberculin Sizable groups of children and young adults have been followed over considerable periods after they became reactors to tuberculin, and an appreciable number have been observed to develop clinical lesions in peripheral lymph nodes, meninges, lungs, bones, joints, and other organs whether or not *pleural effusion intervened In fact,* the majority of such cases did not have pleural effusion Among the students of medicine, University of Minnesota, graduating in the classes of 1930 to 1951, inclusive, 963 became infected while in school or subsequently Pleurisy with effusion occurred in 20, of whom four later had clinical tuberculosis There were 25 of the 963 who developed clinical tuberculosis, in four of whom pleural effusion had intervened

It is the underlying cause and not pleural effusion which determines remote prognosis This underlying cause is the foci of tubercle bacilli deposited in various parts of the body promptly after the initial invasion occurs All of them may remain silent during a person's lifetime On the other hand, at any time after these foci are established one or more of them may provide bacilli for reinfection type of lesions Subpleural ones may cause pleural effusion, those in the central nervous system may cause meningitis, and so on, with all acute and chronic clinical lesions

There is diversity of opinion regarding *remote prognosis* This may be due in part to groups of patients reported For example, if only persons with clinical tuberculosis who give histories of having had pleurisy with effusion some years before are considered, conclusions can be misleading. In the areas from which these persons originated there may have been several others who had undiagnosed effusions or were treated successfully, with no *later tuberculous lesions*

Inclusion of demonstrable primary pulmonary infiltrates as clinical pulmonary disease can be deceiving Except for those who have chest wall lesions and the like, all persons with pleural effusion have antecedent primary infiltrates However, relatively few are large enough, have adequate consistency, or are so located as to be visualized on x ray films From x ray shadows alone it is impossible to determine whether lesions are primary infiltrates or reinfection clinical disease This differentiation can be made only when periodic tuberculin testing has been done or by subsequent observation of the lesions Shadow casting primary infiltrates in any part of the lungs may be obscured from view when fluid *is present and first be observed after it has* absorbed or is aspirated Even then, some such infiltrates are not visualized until they later have sufficient consistency to obstruct x rays In our experience, primary infiltrates per se in children or adults rarely become significant clinically In a group of 236 cases of pleural effusion 55 presented pulmonary shadow-casting lesions while fluid was present or soon after, which proved to be primary infiltrates None subsequently became clinical

It is not unusual for interlobar fluid or that loculated anteriorly or posteriorly to be mistaken for pulmonary lesions from x-ray shadows This also applies to fibrin deposits with or without fibrosis

Among 236 cases with 4620 person years of follow up 23 (9 7%) developed clinical tuberculosis In 10 the lesions were in extrathoracic organs and in 13 they were in the lungs

Prevention

Until recently, prevention of tuberculous pleurisy with effusion was entirely dependent upon avoidance of initial invasion with tuber-

cle bacilli Once the person was infected he was a potential case of pleurisy with effusion This applied to all clinical forms of tuberculosis Evidence is being adduced which strongly suggests that prompt antimicrobial drug treatment for recent converters may prevent meningitis If these drugs will prevent central nervous system lesions and those adjacent to blood and large lymphatic vessels from eroding into brain ventricles subarachnoid space and blood stream it seems possible that they may also prevent subpleural lesions from involving the pleura and causing pleurisy with effusion This has not been determined

RHEUMATIC FEVER

Sero fibrinous pleurisy with effusion occurs with some frequency in rheumatic diseases In fact it is believed that in the neghborhood of 2 or 3% of all such cases are due to this condition It is often immediately preceded by rheumatic pericarditis or pneumonitis

When pleurisy with effusion is first found a history of attacks of rheumatic fever and present other findings of recurrence are important *in diagnosis In most cases the individual is* seriously ill not only because of the pleurisy but also from the involvement of the other organs Occasionally pleurisy with effusion is found with less marked symptoms The condition has become subacute but there is nearly always a history of one or more rheumatic fever episodes or a rheumatic heart condition is present

Rheumatic pleural fluid is usually sterile However this does not rule out tuberculosis *in differential diagnosis inasmuch as laboratory* procedures fail to recover tubercle bacilli in many cases later proved to be tuberculous The occurrence of erythema nodosum just before or during the pleural attack is not helpful because this occurs both in rheumatic fever and tuberculosis The pleural exudate in rheumatic fever is more likely to be sanguinous than in tuberculosis

Treatment

Treatment of rheumatic pleurisy with effusion is that of the general disease plus palliative procedures referable to the pleurisy Sedatives may be administered freely to insure relaxation and sleep and to aid the patient in accepting bed rest Fluid should be aspirated as often as necessary to keep the pleural space as dry as possible This not only avoids accumulation which might result in cyanosis and dyspnea but also prevents fibrin peel from depositing on the pleura which might later require decortication

Prognosis is that of rheumatic fever itself

OTHER INFECTIONS

There are numerous other infections which result in pleurisy with effusion which are less commonly seen In fact practically every disease that causes pneumonitis may result in pleurisy with effusion

Brucellosis

An occasional person with brucellosis may have pleurisy with effusion There is nothing characteristic about the appearance of the fluid and Brucella may or may not be recovered from fluid cultures In the United States the majority of cases of brucellosis occur among *persons in occupations or professions in contact* with cattle and their products particularly veterinarians owners of cattle including members of their families and employees those who work in slaughter houses and butchers in any capacity Therefore the individual's occupation may provide a lead in diagnosis

In organisms not recovered from pleural fluid they may be sought in blood bone marrow and urine The blood agglutination test is dependable

Treatment consists of bed rest and sedatives is indicated Fluid should be aspirated and the pleural space kept as dry as possible Streptomycin or dihydrostreptomycin 0.5 gm intramuscularly twice daily and 0.5 gm aureomycin four times daily for 3 weeks has yielded best results to date

Prognosis is good if treatment is started early

Tularemic Pneumonia

Tularemic pneumonia may be accompanied by pleural effusion History of recent contact with wild animals or an ulcer on the surface of

the body particularly the hands is important The fluid should be examined for Bacillus tularense

The best known treatment for tularemia consists of 0 5 gm of streptomycin or dihydro streptomycin divided into three equal doses and administered intramuscularly every 8 hours for 1 week

Prior to present drug treatment, as many as 20% of persons with tularemic pneumonia died This has been markedly reduced, but it is important to make the diagnosis promptly and administer drugs immediately

Amoebiasis

Persons suffering from amoebiasis, particularly those with liver abscesses, frequently have pleural involvement Endamoeba histolytica may enter the pleural space through lymphatic channels (Fig 4) or by direct extension of the liver abscess through the diaphragm At first, the serous exudate may be sterile, but after the organisms are actually present in the pleural space, empyema develops in more than half of the cases If untreated, the disease extends to the lungs and the pus is eliminated through the bronchi

Diagnosis is made by recovery of Endamoeba histolytica from pleural fluid or other areas of disease

Treatment consists of removal of fluid as indicated Emetine hydrochloride one grain intramuscularly daily for 8 days usually suffices If treatment is started sufficiently early, prognosis is excellent but permanent pleural changes, including adhesions may remain

Fungus Infections

Fungus infections sometimes result in pleurisy with effusion In fact, this occurs in about 15% of persons with actinomycosis The disease usually begins in the peribronchial tissue of a lung and later extends through the visceral pleura Empyema is produced which becomes walled off by adhesion It frequently burrows through the chest wall, involving the ribs, and draining sinuses remain

The diagnosis is made by finding sulphur granules containing gram positive mycelia and growing them in culture

The best-known treatment consists of 600,000 units of penicillin intramuscularly every 6 hours for from 2 to 6 weeks In addition, it is often advisable to remove the infected tissue surgically, including that of the sinus tract

Infections with other fungi, including Histoplasma capsulatum, may involve the pleura

Epidemic Pleurodynia

Epidemic pleurodynia was first described in 1856 Other names applied to this condition are epidemic myalgia, devil's grip and Bornholm disease Usually a knife-like pain, most often over the lower axilla on one side, but occasionally, bilaterally, strikes without warning Pain may be of such character as to be mistaken for that of angina pectoris Referred pain may lead the physician to suspect appendicitis The body temperature is promptly elevated, and in some cases, a chill occurs The temperature ranges from 101 to 104°F and persists for a few hours to a few days

At the onset, other causes of identical symptoms, such as pneumonia and tuberculous pleurisy must be considered Although the pain generally subsides with the fever, a second attack of symptons may occur after 2 or 3 days Ordinarily this is less severe than the first, and usually, the full course of the disease is completed within 10 days In the past, the diagnosis has depended largely upon other cases appearing approximately the same time in the same area

It rarely is fatal and, therefore, little has been known about the pathological process However, it is now known to be caused by Coxackie virus Group B Type 5 Numberous small epidemics have been reported one of the latest being in California beginning in early August, 1956 It first was detected in northern counties of the state and later extended as far south as Fresno, becoming epidemic only in scattered local areas

No drug has yet been found specific for this virus Therefore the treatment still consists of immobilizing the chest wall with tight bandages or adhesive tape and liberal use of sedatives

Epidemic pleurodynia is communicable and, therefore, contagious disease technique should

be employed throughout the full course of the disease In severe cases brief courses of narcotics may be necessary to control pain

"Simple" Pleurisy of Unknown Cause

"Simple" pleurisy of unknown cause applies to cases with attacks of pleural pain with or without other symptoms for which etiology is never determined Pain may persist for a few hours to several days or even a few weeks in the occasional case X ray films of the chest are unrevealing with reference to location of an area of disease presence of effusion etc There may or may not be elevation of body temperature It is believed that in many such cases areas of pneumonitis develop at the periphery of the lung so situated or too small or without adequate consistency to cast shadows visible on the x ray film The pleura becomes involved fibrinous pleurisy develops and the condition heals Treatment consists of applying a tight binder or adhesive tape around the chest so as to reduce the movement of the chest wall as much as possible mild sedatives and as near complete rest as possible until symptoms disappear

It is believed that the majority of such cases undergo complete healing However no record has been found of a sufficiently large number observed over a period of decades to determine ultimate prognosis If the individual reacts to tuberculin there is possibility that the apparently simple condition is tuberculous Inasmuch as tuberculosis is a disease of remissions and exacerbations all such persons should be examined periodically long after the pleural episode has subsided

INFECTIONS WITH PYOGENIC BACTERIA

Pyogenic bacteria frequently attack the pleura secondary to pulmonary infections Prior to the advent of antimicrobial drugs pneumococci often involved the pleura and resulted in empyema during and following attacks of lobar pneumonia Many such pleural infections were controlled by the body s defense mechanism and did not pass beyond the fibrinous pleurisy stage with resulting adhesions However in approximately 4 or 5% empyema developed When empyema occurred following the attack of pneumonia the body temperature again became elevated severe chest pain developed and the leukocyte count was again increased These findings promptly called attention to the development of empyema whereas when this condition developed while pneumonia was at its height the empyema was often overlooked

If aspirated early in the course of the disease the fluid is usually amber colored slightly turbid and thin However within 2 or 3 weeks it is greenish pus The early fluid should be studied bacteriologically since in a small percentage it is sterile and is quickly absorbed without progressing to empyema In the remainder of cases the early fluid contains numerous polymorphonuclear leukocytes and bacteria

Needle aspiration suffices in many cases If rib resection becomes necessary it should not be done until the mediastinum is well fixed It should also be determined whether broncho-pleural fistula is present by introducing into the empyema cavity 2 cc of a 1% solution of aqueous gentian violet This will appear in the sputum within one or two days if fistula is present Most cases formerly required surgical drainage With immediate and adequate administration of crystalline penicillin G or procaine penicillin in water intramuscularly 300 000 to 600 000 units every 12 to 24 hours for 5 to 7 days pneumococcal pneumonia now is usually controlled and empyema is prevented

Hemolytic Streptococci

Hemolytic streptococci causing pneumonia frequently involve the pleura and result in empyema Such patients usually are extremely toxic as bacteriemia frequently co exists Organisms are found in the pleural exudate During World War II the United States Army Empyema Commission headed by Evarts Graham observed that many deaths resulted from empyema when open drainage was instituted too early This commission found that until the patient s vital capacity returned to a safe level it was best to employ needle aspiration When the vital capacity returned to a safe level and there was evidence that the

mediastinum was fixed, the number of deaths following surgical drainage was markedly reduced. Since that time it has been strongly recommended that in the early course of empyema only needle aspiration be employed. Open drainage instituted too early allows air to enter the pleural space and the mediastinum shifts markedly to the opposite side with such encroachment upon the uninvolved lung as to frequently result fatally. For streptococcal infection, penicillin should be employed in the same dosage as in pneumococcal empyema. From 100,000 to 200,000's of crystalline penicillin in 200 cc. of physiological saline solution should also be introduced every 48 hours after aspirating pus.

This type of empyema has also been markedly reduced in prevalence by treating streptococcal pneumonia and bacteremia early with antimicrobial drugs.

Calcification of the Pleura

Calcification of the pleura may occur in small or large areas. This condition usually is seen in persons who have had pleural fluid and more often in those who have had tuberculous empyema or hemothorax. Even large calcium plaques usually cause no symptom and require no treatment. However, in the occasional case, pockets of tuberculous empyema remain or recur. Treatment of this complication has been facilitated with the advent of antimicrobial drugs and chest surgery.

STERILE INFLAMMATORY PLEURISY

Pulmonary Infarction

Subpleural infarcts result in inflammation of the overlying pleura. Fibrinous exudate promptly appears, and later, serous exudate accumulates in the pleural space, which usually contains blood. When a sufficient amount of serous exudate accumulates, pleural pain disappears. Aspirated fluid, because of its blood content suggests the presence of malignancy or less likely tuberculosis. However, the fluid is sterile and malignant cells are not found.

In most cases, no treatment is necessary. However, aspiration is indicated if pressure symptoms appear.

Occasionally, pulmonary infarcts become necrotic and liquify, resulting in lung abscess. Rarely, such an abscess ruptures through the visceral pleura and results in *putrid empyema* and the findings are those of pyopneumothorax.

Traumatic Pleurisy

A blow or other injury to the surface of the chest may result in hematoma developing subpleurally whether or not rib fracture occurs. If severe enough, the injury may result in hematoma beneath the visceral pleura. Over such hematomata fibrin deposits on the pleura and serous exudate may accumulate in the pleural space. If a sufficient amount of fluid accumulates, it is seen on x-ray film or fluoroscopy. Ordinarily, only palliative treatment of the pleural condition is necessary. Occasionally ruptured blood vessels result in hemothorax.

Post irradiation Pleurisy

Along with pneumonitis caused by intensive x-ray treatment, the pleura may become involved. Usually this consists only of fibrosis, but occasionally, pleural effusion appears. The fluid is sterile and usually resorbs gradually without treatment.

PLEURAL FLUIDS OF NONINFLAMMATORY ORIGIN

Pleural Transudates

Pleural *transudates* due to venous passive congestion usually occur in persons with congestive heart failure. There has been no explanation as to why the fluid accumulation is frequently unilateral and more often, on the right side. If not already known to exist, usually when pleural fluid is found, some *form of heart disease* is detected. However, if this is not found or is not sought, fluid should be aspirated *for study*. It is usually thin, clear and straw-colored, with less than 500 lympho-

cytes per cu mm Pathogenic micro organisms and malignant cells are found in uncomplicated cases In most persons no treatment is indicated as the fluid absorbs when the heart condition is adequately treated However when a large volume of fluid is present and dyspnea and orthopnea are severe removal of fluid together with treatment of the heart *condition may bring prompt relief If fluid* continues to accumulate aspiration should be done before it causes marked pressure symptoms and reduced vital lung capacity

Neoplasms invading the mediastinum may block pulmonary lymphatics and occasionally veins so they become distended and serous transudate passes through the visceral pleura and accumulates in the space Hodgkin s disease may also result in this situation as well as carcinoma which infiltrates mediastinal lymphatics so as to prevent the flow of lymph from the lungs

Usually fluid accumulates rapidly and pressure symptoms soon are in evidence The final diagnosis is made by discovery and classification of the mediastinal tumor

Frequent aspirations may be required If Hodgkin s disease is responsible deep x ray treatment may bring temporary relief This may also be true if radio sensitive carcinoma is responsible

More often than is generally appreciated *cirrhosis of the liver* results in accumulation of pleural transudates which is nearly always on the right side Aspirated fluid proves to be a clear transudate Only with great rarity is it necessary to remove fluid because of pressure symptoms

Any condition that causes *hypoproteinemia* may result in accumulation of transudate in a pleural space Of these nephrosis is most often responsible The mechanism of pleural effusion in nephrosis is simply that of transudation of water and electrolytes out of the capillaries for lack of sufficient colloid osmotic pressure to hold the liquid in the vessels Fluid accumulations are often bilateral

Treatment is that of the nephrotic syndrome except aspiration of fluid may be necessary when pressure symptoms appear Diuretics and restriction of salt are helpful Administration of human blood proteins in large amounts is of at least temporary value

HEMOTHORAX

This refers to gross blood in the pleural space and must be distinguished from pleural exudate containing blood as is frequently seen *in malignancies pulmonary infarcts and occa*sionally tuberculosis The blood is bright red if aspirated promptly after bleeding occurs However if aspirated a week or two later it appears brown Severe *injury to the chest wall or deeply penetrating stab or bullet wounds* may result in extensive bleeding into the pleural space from an intercostal or internal mammary artery or from the lung itself

A small amount of fresh blood in the pleural space usually does not result in significant symptoms If continuous bleeding occurs and a large volume of blood enters the pleural space shock may be in evidence within two or three hours with marked dyspnea and cyanosis Such bleeding may result fatally in a short time if not recognized and treated promptly On physical examination the findings are those of any other fluid of large volume in the pleural space except that in hemothorax they develop rapidly Small hemothorax requires no treatment as the blood soon absorbs Larger amounts of from 500 to 1 000 cc may also absorb However it is usually thought best after bleeding stops to aspirate so as to prevent later complications such as calcification or fibrosis of the pleura

If the bleeding continues as evidenced by pressure symptoms and increasing shock intravenous plasma should be administered continuously Auto transfusion of the blood from the patient s cavity may be started and continued If the bleeding does not stop and it is suspected that it is coming from the lung air may be introduced into the pleural space as blood is removed for transfusion Often 1 000 cc of air is adequate to stop the bleeding If this does not suffice prompt arrangement must be made for surgery This may be facilitated by thoracoscopic examination in an effort to determine the location of bleeding Exploratory thoracotomy may be necessary

Only rarely does infection complicate hemo

thorax However antimicrobial drugs should be employed as a precautionary procedure

Occasionally thoracic *aortic aneurysm* ruptures into a pleural space usually on the left side resulting in immediate death Again such an aneurysm may slowly leak blood into the pleural space This may be intermittent or continuous A sufficient *amount may accumulate* to result in pressure symptoms When the diagnosis is made prompt consultation should be had with a chest surgeon

Occasionally a pulmonary malignant process results in hemorrhage into a pleural space Usually only palliative measures are indicated

CHYLOTHORAX

Chylothorax often results from injuries which rupture the thoracic duct slightly above the diaphragm In some cases this has been attributed to sudden violent hyperextention of the spine More recently a number of cases have been reported following chest surgical procedures Such injuries allow chyle to enter the retropleural area which later finds its way into the pleural space

Involvement of the mediastinum by Hodgkin's disease lymphosarcoma etc may result in obstruction of the thoracic duct Distal to the obstruction there may be rupture of the duct or slow leakage of chyle with accumulation in the pleural space

On examination evidence of pleural fluid is *found which does not differ from other* fluid accumulations in the pleura However the diagnosis is readily made from aspirated fluid which has the general appearance of milk with 1 to 2% fat content

In recent years there has been a strong tendency to keep the pleural space as free from chyle as possible by aspirations as indicated This may be done with needle and syringe or tube drainage with suction Various surgical procedures have been considered including anastomosis of the duct to a vein anastomosis of the cut ends or repair of the wall Although it has been repeatedly stated that surgery can be of no avail in recent years a number of cases of chylothorax have been treated successfully by ligation of the thoracic duct immediately above the diaphragm

When obstruction is caused by lymphoblastoma deep x ray therapy has been employed with the thought of temporarily reducing the obstruction of the thoracic duct

In the past about 50% of the cases of chylothorax recovered This may be expected to increase with present and proposed surgical *techniques for those due to trauma*

TUMORS OF THE PLEURA

(See Chapter 19)

PNEUMOTHORAX

Trauma has long been known to result in pneumothorax Riolan (1648) Littre (1713) Meckel (1759) and others in the F
and Nineteenth Centuries reported
pleural cavity following trauma In 1
called attention to five cases found
ropsy He coined the term pneu
Air may reach a pleural space thro
parietal pleura as in stab or bullet
foreign bodies in gus or bro
during bronchos agoscopy

ing needle aspiration of fluid air may gain entrance to the space
Most freque found in the pleural
cavity as a re ful induction in the
treatment ar of disease
Air may ur ty through
e visceral p es
ommu amifica
or air permits
enter th for
ose may

puncture the visceral pleura Resuscitation of newborn infants passing a bronchoscope administering intratracheal anesthesia etc are sometimes responsible

Areas of *disease* may enter a pleural space through the chest wall including those in the *esophagus stomach trachea and subphrenic* abscess

Hewson (1767) apparently was first to mention the possibility of entry of air into a pleural space through perforation of pulmonary diseases It is now known that both acute and chronic disease may so damage the visceral pleura as to permit the escape of air into the pleural space

The term *spontaneous pneumothorax* has been reserved for those cases in which disease or defect of the pleura permits air from the lung to enter the pleural space Earlier in the evolution of our knowledge of spontaneous pneumothorax this condition was usually recognized in persons who had pulmonary disease demonstrable during life or at necropsy More cases were reported due to pulmonary tuberculosis than to any other disease probably because of its prevalence and inadequacy of differential diagnostic procedures so that many nontuberculous pulmonary conditions were classified as tuberculous Biach (1880) collected 986 cases of spontaneous pneumothorax from the literature and from the records of three Vienna hospitals and found tuberculosis reported as responsible in 77 8% As late as 1931 Palmer and Taft stated that among adults from 80 to 90% of the cases of spontaneous pneumothorax were due to tuberculosis

As time passed there was an increasing number of persons reported with spontaneous pneumothorax who did not react to tuberculin tubercle bacilli were not recovered and no evidence of tuberculosis was then or later obtainable Since the cause was not determined this condition was referred to as *idiopathic spontaneous pneumothorax*

This was frequently seen in young men who remained in good health so there were few opportunities to make postmortem examinations However in 1932 and 1933 Kjaergaard reported five of his own cases and six others from recent literature in which he described the etiology In one type a valve is formed by emphysematous tissue in another by congenital valve vesicle and in the other by scar tissue He designated the condition *spontaneous pneumothorax simplex* Kjaergaard pointed out that frequently spontaneous pneumothorax in an apparently healthy person has no relationship to tuberculosis He expressed the opinion that individuals with this condition should be spared loss of time and expense of sanatorium treatment as well as fear of tuberculosis

Kjaergaard s observations have been adequately confirmed and it is now recognized that *simple spontaneous pneumothorax* is usually due to congenital or acquired defects in the lung or pleura resulting in emphysematous blebs (bullae air vesicles etc) which rupture in one or more places so air gains admission to the pleural space Adhesions between the parietal and visceral pleurae may also result in rents in the latter

In 1934 Hamman described spontaneous interstitial emphysema of the lungs He believed it was due to rupture of pulmonary alveoli with the escape of air into interstitial tissues The cause of this condition was not known but he suggested that an alveolar wall here and there may become attenuated and weakened without known reason This could be due to developmental defects previous disease or present disease too slight to be detected In any event, when a large amount of air escapes in this manner it may dissect along the connective tissue bands surrounding blood vessels and form blebs on the pleura which in turn may rupture and cause spontaneous pneumothorax

Among our 115 reported cases 73% occurred *between the ages* of 15 and 29 years The youngest was 1 and the oldest 64 years old This age incidence has been a common observation of numerous authors but no entirely satisfactory explanation has been offered

Many authors have observed much more frequent occurrence of simple spontaneous pneumothorax among men than among women In our group 98 (85%) were men This sex difference has not been satisfactorily explained

Diagnosis

Symptoms at onset vary from those unrecognized by the individual to those of extreme

severity Most frequently the initial symptom is sharp pain This may occur over various parts of the involved side including upper and lower axillae precordium shoulder and in some cases substernal regions Not infrequently the pain radiates down the arm In some cases the initial pain is localized over the epigastrium Usually pain precedes dyspnea In some cases severe dyspnea does not occur In others shortness of breath is the first symptom One patient stated that he felt his air was suddenly shut off—pain followed Fever rarely appears In most cases severe symptoms begin to subside within a few hours and soon disappear

In about one third of the patients the first symptoms are mild such as slight aching in a shoulder slight chest pain on changing posture *or occasionally on respiration or a feeling of* oppression or slight pressure on the involved side No symptom is pathognomonic

Activity of the individual at the time of onset affords no help in diagnosis A large variety of activities at the time the first symptoms have been observed varying from strenuous work to sound sleep In our group of 115 only 25 were doing strenuous work while 31 were asleep or engaged in slight activity such as reading at the time of onset of symptoms

The findings on *conventional physical examination* depend upon such factors as degree of collapse and how soon the individual is seen In severe cases examined within an hour *or so after onset inspection reveals evidence of* cyanosis anxious expression and in some signs of shock Respiratory rate is accelerated and the movements of the chest wall on the involved side are definitely limited If intrapleural positive pressure is present the intercostal spaces may bulge At the opposite extreme when only a small amount of air has reached the pleural space the only finding on inspection may be slight limitation of movement of the chest wall

Percussion with an underlying extensively collapsed lung usually reveals a resonant or even tympanitic note When there is marked tension the chest wall acts like an overstretched drum and cannot vibrate Thus the percussion note becomes muffled and at time approaches dullness In small pneumothoraces there may not be enough air present in the pleural space to alter the percussion note

When the lung has collapsed to 50% or more of its volume breath and voice sounds are usually faint or entirely absent In small pneumothoraces all auscultatory findings may be normal

The conventional physical examination is of almost no aid when small amounts of air such as 200 to 300 cc are present in the pleural space

Fluoroscopic and x ray film inspection of the chest play an important role in detecting unsuspected and confirming questionable cases and determining the degree of collapse as well as appreciable displacement of the mediastinum and diaphragm X ray inspection reveals a mantle of decreased density at the periphery *of the lung with absence of lung markings and* demarcated from the atelectatic lung margins When only a small amount of air is in the pleural space it may be completely overlooked by x ray inspection Again air may be pocketed in front or back of the lung so it is not visualized on the usual posteroanterior exposure

Among our 115 cases in the initial attack the degree of collapse was less than 25% in 15 In seven the collapse was approximately 25% in 8 33% in 7 40% in 33 50% in 11 from 60 to 75% and in 34 the collapse was complete

The diagnosis of simple spontaneous pneumothorax is made by correlation of history conventional physical signs and x ray shadows In some cases one or more of these is misleading and therefore differential diagnosis may be difficult From symptoms alone simple spontaneous pneumothorax has been diagnosed as pneumonia intercostal neuralgia pleurisy coronary disease acute heart failure pericarditis and even perforated gastric lesions

The findings on conventional physical examination may be confused with those of large pulmonary cavities marked upward displacement of one side of the diaphragm with large collections of gas in the digestive organs diaphragmatic hernia gaseous sub diaphragmatic abscess pulmonary aplasias and pulmonary cysts

Treatment

Many cases of simple spontaneous pneumothorax require no treatment except sedation at the beginning and reduced physical activity. For others bed rest at home or in a hospital is advisable for a few days to a few weeks depending upon degree of collapse and rate of re-expansion. The pleural rent soon closes and the lung re-expands without incident in most cases. As the lung re-expands activity may be increased gradually and the majority of cases treated by bed rest are able to resume normal living in a few days to a few weeks. Throughout the re-expansion period the individual should be instructed to report promptly the appearance of any symptom such as pain, shortness of breath or pressure. Frequent fluoroscopic or x-ray film inspections should be made until the lung appears to be completely re-expanded and for some weeks thereafter.

In uncomplicated cases aspiration of air either by needle or catheter is neither indicated nor advisable. The creation of abnormal negative pressure in the pleural cavity may keep the pleural rent open.

Complications

A small amount of *pleural* fluid may accumulate in approximately 35 to 40% of cases which absorbs without incident. Only rarely does a moderate to large amount of fluid appear in uncomplicated cases. When fluid in small or larger amount does not absorb promptly it should be removed by needle or catheter as frequently as necessary to keep the pleural surfaces as dry as possible. Otherwise the lung may not re-expand promptly as fibrin is likely to deposit on the pleural surfaces, greatly delaying and even preventing re-expansion, after which decortication may be necessary.

Occasionally when the visceral pleura ruptures blood vessels are torn with bleeding into the pleural cavity. This may be in small or large quantity. In all cases of *hemopneumothorax* blood should be aspirated as often as necessary to keep the pleural space as dry as possible. If the hemorrhage persists unduly long or a dangerous amount of blood is being lost, bleeding points should be closed surgically and at the same time the rent in the pleura repaired. In severe cases blood transfusions may be necessary.

Spontaneous hemopneumothorax occurred in nine (7.8%) of our cases.

Tension Pneumothorax

Occasionally when pleural rupture occurs a flap remains which acts as a one-way check valve. Thus air enters the pleural space on inspiration but closure of the valve prevents its escape on expiration with the development of positive pressure. This situation immediately becomes an emergency as pressure may result in marked mediastinal displacement with severe embarrassment of respiratory and cardiac function. If the condition is not recognized death can occur in a short time.

If diagnosis is made in time prompt relief is observed by thrusting an 18 gauge needle through the chest wall. Enough air escapes to remarkably reduce the pressure in a few seconds. It may then be necessary to pump air from the pleural cavity but high negative intrapleural pressure should be avoided. After the initial aspiration the patient must be kept under constant observation for pressure symptoms. If these occur other aspirations may be necessary. In some cases after the needle is removed air accumulates so fast and aspirations are required so frequently that an indwelling needle or catheter and check valve are advantageous to provide continuous escape of air until it no longer accumulates sufficiently to cause pressure. At all times high negative intrapleural pressure should be avoided.

If the lung does not re-expand and positive pressure continues to develop after aspiration is discontinued it may be necessary to close the opening in the visceral pleura surgically.

Occasionally *bilateral simple spontaneous pneumothorax* is present when the first examination is made. Among persons who have recurrent simple spontaneous pneumothorax some have alternating attacks on the two sides and occasionally both lungs are found partially collapsed simultaneously. Bilateral collapse has occurred in 9 of our 100 traced cases.

Recurrence

Brock has reported the largest and best presented series of cases of recurrent and

chronic spontaneous pneumothorax from which he draws excellent conclusions from the standpoints of diagnosis and treatment

We have kept in touch with or have recently traced 100 of our cases whose initial episodes occurred from 1 to 29 years ago, and found that 71 have had no repetition while 17 have had one recurrence all on the original side except two Twelve have had more than one recurrence, ranging from two to many In five of these, all recurrences were on the original side

Since 29 of this group have had one or more recurrences everyone who has had an initial attack should be advised of the possibility of others and how to proceed in the event symptoms of tension pneumothorax begin to appear

Treatment of recurrent simple spontaneous pneumothorax depends upon a number of factors such as frequency and severity of attacks

Apparently an attack of simple spontaneous pneumothorax usually does not result in symphysis of the pleurae When spontaneous pneumothorax has recurred more than once we have usually recommended procedures to prevent further attacks For such cases it is now advised that chest surgeons explore and close rents in the pleura, remove pleural blebs in evidence and produce slight irritation of pleural surfaces by gentle friction with a sponge to insure pleurodesis

Prevention

As yet no method has been devised to determine in whom this condition may occur since in most persons who have it x-ray inspection fails to reveal evidence of pleural blebs either before the attack or after the lung is re-expanded In an occasional person who has not had an attack, however, pleural blebs or bullae may be sufficiently large to be detected on x ray films This does not necessarily indicate that such persons will have spontaneous pneumothorax However, the potentiality might be reduced by removal of such blebs as can be found

It is not known what causes blebs to rupture We have seen persons who have had spontaneous pneumothorax onsets when engaged in most strenuous physical work and others while they were relaxed in sound sleep as well as those engaged in various intermediate degrees of activity It appears that in some cases the visceral pleura becomes so thin or the pressure so high in the blebs that the increase in negative intrapleural pressure on quiet inspiration is adequate

In persons who have had one or more attacks of spontaneous pneumothorax one should always issue a warning of the possibility of subsequent attacks and the advisability of prompt contact with the physician with the onset of symptoms Even a minor degree of shortness of breath may indicate that a check valve is present and positive intrapleural pressure is developing Delay can prove fatal in a short time

Anyone who has had an attack of spontaneous pneumothorax should be advised against *high altitudes* especially in airplanes except in pressurized cabins and where oxygen can be administered Persons recovering from spontaneous pneumothorax but in whom the lung is not completely expanded, no matter how small the mount of air still demonstrable, should also be warned against airplane travel except in pressurized cabins The volume of air in a pleural cavity increases with altitude Three thousand cc in a pleural cavity at sea level assumes the volume of 3720 cc a mile above Therefore, a person with pneumothorax may be in distress at 1 mile and his life jeopardized at higher altitudes At 18,000 feet the volume of air is doubled and at 34,000 feet, quadrupled

Many physicians recall emergencies that were created early in World War II by transporting spontaneous pneumothorax cases by airplane The problem was of such magnitude that in July 1944 the National Research Council issued an excellent special pamphlet prepared by J J Waring, Denver, Colorado on the diagnosis and management of spontaneous pneumothorax This was made available to our military medical officers everywhere

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CHAPTER 23

Diseases of the Diaphragm

J Arthur Myers MD

POSITION

Of all muscles of the human body the diaphragm is second only to the heart in importance Its development innervation physiology change of position due to posture etc have been presented in detail by Scammon Rasmussen and Visscher Abnormalities in the abdomen chest and central nervous system may cause lowering or elevation of the mean position of the diaphragm For example a low position may be observed in acute diaphragmitis from any cause or when the phrenic nerve anywhere from its central origin to its peripheral branches is irritated as may occur in encephalitis tetanus tetany and singultus with peritonitis Again the diaphragm is low in the presence of visceroptosis and asthenia Conditions within the chest such as pleural fluid pneumothorax emphysema and asthma frequently result in a low position of the diaphragm

Abdominal conditions such as peritoneal fluid or air gas in the digestive tract tumors and pregnancy may cause marked elevation of the diaphragm Conditions within the chest such as atelectasis extensive pulmonary fibrosis and adhesions are often responsible for a high position of the diaphragm Moreover interruption of a phrenic nerve congenital muscular defects and myasthenia gravis may result in marked diaphragmatic elevation The reflex protective mechanism often results in its elevation on the side of recent pulmonary disease

DIAPHRAGMITIS

PRIMARY DIAPHRAGMITIS

Trichiniasis sometimes causes primary diaphragmitis The organisms enter the diaphragm as is true of other muscles of the body and may produce serious myositis Indeed the involvement together with that of the intercostal muscles may become so extensive as to cause death Scurvy in the terminal stages often results in induration of muscles rupture of fibers and hemorrhage This has also been seen in the diaphragm among those who have suffered from severe dyspnea and discomfort over the lower part of the chest even though lung lesions are not present

The etiology of *acute diaphragmitis* also known as Hedblom's syndrome is not known It consists of acute inflammation with swelling of the muscle fibers and infiltration of leukocytes into the tissues The inflammation may be limited to the muscle or extend to its serous coverings When the diaphragmatic pleura is involved fluid may accumulate and adhesions later develop between it and the visceral pleura even to the point of obliterating the cardiophrenic and costophrenic angles In severe cases destroyed muscle fibers are replaced by fibrous tissues to such an extent that the diaphragm partially loses its ability to function and appears flat rather than dome shaped on x ray inspection In arriving at a diagnosis Joannides found the condition is usually preceded by a chill 24 to 48 hours be

e the onset of other symptoms Some of his tients gave histories of having had attacks of ute rhinitis immediately preceding the dis se After the chill the next symptom usually nsists of pain over the costal margins and in e shoulder region of the involved side which intensified on inspiration

The reflex protective mechanism may re lt in partial immobilization of the lower part the chest wall as well as the diaphragm In e beginning there are no abnormal stetho opic findings or x ray shadows over the lungs though these may later appear if the disease tends to the lungs Spasm of the transversus dominis muscle may occur due to reflex or actual extension of the condition into the bers of this muscle The polymorphonuclear ukocytes range from 9 000 to 20 000 per cu m of blood after symptoms are well estab hed

Diaphragmitis must be differentiated from nditions causing pressure on the diaphragm ich as spontaneous tension pneumothorax tificial or spontaneous pneumoperitoneum ate conditions of the abdomen which ex nd to the diaphragm or the transversus ab ominis muscle intercostal herpes zoster leurodynia acute spasm of the diaphragm ritation of the phrenic nerve in the mediasti um basal pneumonitis scalenus syndrome nd cervical ribs Joannides is of the opinion at acute primary diaphragmitis occurs much ore frequently than was formerly believed le has reported a sizable group of patients in hom all other causes of symptoms were ap arently excluded Spasm of the transversus bdominis muscle together with other symp oms and leukocytosis he believes has often d to erroneous diagnosis of appendicitis and holecystitis

There is no specific treatment for this condi on Partial relief from pain may be obtained y administration of sedatives and application f a tight bandage or adhesive tape to reduce he movement of the chest wall on respiration

In mild cases the immediate prognosis is ood and the symptoms disappear within a ew days but may recur with changes of weather The disease may extend however o as to involve the diaphragmatic pleura re ulting in pleural effusion and even empyema It may then extend to the visceral pleura and result in pulmonary involvement Again the diaphragmatic peritoneum may be in volved Jeannides reported such a case that caused abscess of the liver which later rup tured through the diaphragm into the pleural cavity with a resulting effusion containing characteristic liver tissue In nearly all cases apparently the diaphragm is impaired by the replacement of destroyed muscle fibers by fibrous tissue

SECONDARY DIAPHRAGMITIS

Secondary diaphragmitis is caused by dis ease conditions immediately above or below the diaphragm which extend to this organ and result in inflammation Pneumonia is a com mon cause In cases of bronchial pneumonia diaphragmatic changes are usually slight and recovery is complete However in basal lobar pneumonia marked diaphragmatic changes may occur and in fatal cases postmortem ex amination often reveals waxy degeneration of muscle fibers

Inflammation of the pleura often extends to the diaphragm It is especially dangerous to permit fluid particularly when purulent to remain in the pleural cavity When this oc curs approximately five out of six cases de velop impairment of the diaphragm which usually is permanent Tuberculosis frequently attacks the diaphragm Of all muscles of the body the diaphragm is most frequently at tacked by this disease Not infrequently tu bercles are found within the muscle itself

The weight of a medium or large pleural effusion may seriously damage the diaphragm particularly if it is allowed to exist for weeks or months Indeed, in such cases its convexity may face the abdomen because of loss of func tion and elasticity plus the weight of the fluid This should be kept in mind when fluid ac cumulations appear in persons being treated by artificial pneumothorax When fluid is allowed to remain in the pleural space there is a strong tendency for fibrin to deposit and ad hesions to form particularly in the costo phrenic angles and between the pericardium and the diaphragm These tend to fix the dia phragm in an abnormal position and thus

markedly impair its function In extreme cases of diaphragmatic adhesions the heart may be markedly displaced and lose its normal contour to such a degree as to impair its function

In some pulmonary conditions, particularly chronic tuberculosis, dyspnea is out of proportion to the amount of pulmonary involvement In such cases it may be the impairment of the diaphragm which is partially responsible for the dyspnea In advanced pneumoconiosis bilateral adhesions may result in marked restriction of the diaphragmatic excursion which accounts in part for the dyspnea experienced in some cases

The diaphragm is richly supplied with lymphatic vessels and channels into which lymph from some parts of the abdomen drains Therefore, it is not uncommon for it to become infected by bacteria which originate in the abdomen

Occasionally primary tumors develop in the diaphragm Metastases to this organ are not uncommon, particularly from primary malignancies in the stomach

SUBDIAPHRAGMATIC ABSCESS

ETIOLOGY

Infection in the abdomen may result in subdiaphragmatic abscess (subphrenic peritonitis and subphrenic abscess) Simple abscess usually occurs on the right side, between the liver and the diaphragm The most common cause is appendicitis from which the organisms are usually carried to this region by way of the lymphatics Second to appendicitis, suppurations within the liver itself, such as amoebic abscess, hydatid cyst, and infection of the gall bladder, are the most common causes Occasionally disease of the uterine tubes, the pancreas, or the retroperitoneal region is responsible. When on the left side, abscesses are most frequently caused by perforated gastric and duodenal ulcers, and occasionally by perforated ulcers in the colon and by gastric cancer In rare cases subdiaphragmatic abscess results from disease above the diaphragm, such as empyema and pneumonia These abscesses vary in size from that of a large walnut to that with a capacity of a quart In the pus one may find streptococci, staphylococci, colon bacilli, pneumococci and in some cases, tubercle bacilli and other organisms, as are found in abscesses in other parts of the body Only occasionally do right subdiaphragmatic abscesses contain air, but air is found in the majority which occur on the left side

DIAGNOSIS

In the early course of development, the diagnosis is difficult for subdiaphragmatic abscesses are usually located beneath the dome of the diaphragm but above the lower margin of the lung so that pulmonary tissue is interposed between them and the surface of the body Because of their location with consequent pressure on the diaphragm, approximately 8% of them give rise to thoracic symptoms Indeed, in some cases, particularly those that develop slowly, the first symptom may be mild or severe pain over the lower part of the chest which often radiates to the shoulder, as is true when the diaphragm is irritated from any other cause Again, the pain and tenderness may be limited to the upper abdominal quadrant Before complications occur it is often difficult to determine whether the condition lies within the thorax or the abdomen

Since most simple abscesses localize near the spinal attachment of the diaphragm on the right side abnormal physical signs may be elicited over the lower and posterior parts of the right side of the chest The diaphragm is elevated and partially or completely immobilized Therefore, it is difficult to determine whether the decreased movements of the chest wall, the diminished tactile fremitus, the changes in the percussion note, and the suppression or absence of breath sounds are due to pleural fluid or subdiaphragmatic abscess Indeed, clear pleural fluid may be aspirated, but this does not account for the leukocytosis and the symptoms of suppuration X ray inspection is of great value before thoracic complications develop, as it shows the outline of the diaphragm, beneath which may be seen an

area of density which accounts for its elevation and decreased excursion. Occasionally subdiaphragmatic abscess develops more anteriorly than above described, hence the location of pain and abnormal physical signs are correspondingly changed. If an exploratory needle puncture is done, one must use extreme caution that the needle does not pass through the lower part of the pleural space so as to allow pus to enter and produce empyema.

COMPLICATIONS

Serious complications may occur if these abscesses are not recognized and treated promptly. They enlarge and push the diaphragm upward and the liver downward and perforate the diaphragm so as to infect the pleural space and thus produce empyema. Occasionally they actually perforate the lung and the contents are expectorated as in the case of pulmonary abscess. Again the infection may extend to the liver where multiple fatal abscesses are produced. When perforation of the diaphragm occurs so as to result in empyema or pulmonary changes, the findings over the chest do not differ from those of the same conditions from other causes. However, this complication adds greatly to the difficulty in making a diagnosis of the original condition.

TREATMENT

The treatment of subdiaphragmatic abscess consists of surgical drainage at the earliest possible moment after the diagnosis is established if antimicrobial drugs fail.

PROGNOSIS

The prognosis has improved with modern treatment. Indeed nearly all cases resulted fatally prior to the advent of antimicrobial drugs and surgical drainage.

DIAPHRAGMATIC HERNIA

TRUE HERNIA

In true diaphragmatic hernia, the pleura, the peritoneum, or both remain intact while parts of the abdominal contents extend through the diaphragm into the thorax within the sac formed by one or both of the serous coverings of the diaphragm. This condition may be due to defects in the muscular layer of the diaphragm through which the abdominal contents pass under pressure. While such hernias may occur in any part of the diaphragm, about 70% occur at the esophageal hiatus.

In apparently normal persons, hiatus hernia has been found in from 1.3 to 8%. It is best demonstrated on roentgenograms of the stomach following barium swallow with the subject in the Trendelenburg position. Some of these hernias are congenital while others are caused by trauma to the chest or abdomen, as well as conditions that increase intra-abdominal pressure, including ascites, chronic constipation, obesity, and pregnancy. Persons in the upper age bracket are more prone to this condition because of decrease in fatty and elastic tissue at the hiatus.

Brown *et al.* used the term "compound diaphragmatic hernia" when more than one organ has passed through the involved foramen (not including the traumatic type). Although compound hernias are infrequent, they may eventually result in severe cardiorespiratory embarrassment and later result in death. This is in addition to the wellknown obstructive phenomena of the stomach or bowel. While involvement of the colon in non-traumatic hernia is not common, Brown *et al.* reported 5 cases to add to the 29 reported in the literature up to 1951. They consider correct diagnosis and surgical correction of the defect in such massive herniation as mandatory to reduce pulmonary disability. Compound diaphragmatic hernias involving the foramen of Morgagni and the foramen of Bochdalek are also infrequent.

Defects of the diaphragm occur about six times more frequently on the left than on the right side. Therefore hernias are more fre-

quently found on the left side On the right side the liver is so placed as to serve as a protection to the diaphragm

In true simple diaphragmatic hernia, symptoms may be entirely lacking, and the condition is revealed when an examination is made for another purpose or at postmortem In other cases, pain may be experienced in the region of the epigastrium or just above the ensiform cartilage This is most noticeable when the individual is lying in bed Symptoms may cause one to think of gallbladder disease, ulcer, or malignancy In many cases, no physical sign can be detected except those revealed by x-ray film particularly after barium is introduced into the gastro-intestinal tract

When diaphragmatic hernias are discovered accidentally and are not causing symptoms no treatment is necessary However, those which are large and are producing significant symptoms may require surgical treatment

FALSE HERNIA

False congenital diaphragmatic hernia is usually due to arrest of development of the pleuroperitoneal membrane which results in congenital absence of a part of the diaphragm In extreme cases death usually occurs in fetal life Such congenital defects occur much more frequently on the left side than on the right and permit the abdominal organs, such as the stomach and parts of the intestine and occasionally the spleen, the pancreas and the left kidney, as well as a portion of the liver, to enter the pleural sac Indeed, in extreme cases most of the pleural sac is occupied by these organs Such hernias vary in extent from this extreme to those with defects in the diaphragm which admit only small parts of the abdominal contents They are usually diagnosed with ease by x ray inspection after barium has been introduced into the gastro intestinal tract Many of them are detected only when an examination is being made for some other reason or at postmortem

TRAU[illegible] A

(See Chapter 2[illegible]

ELEVATION (EVENTRATION) OF THE DIAPHRAGM

This condition, also referred to as dilatation, high position, insufficiency, and relaxation, is an abnormally high position of one half of the diaphragm, either congenital or acquired Although an authentic case was described by Petit in 1774, the term, eventration, was not applied until 1849 The high position is permanent and the diaphragm is intact However, the abdominal contents are placed high and in part occupy space which normally would be the thoracic cavity In congenital cases the condition is probably due to failure of the diaphragmatic musculature to develop on one side, and instead of the muscle there exists only a thin membrane The pleural and peritoneal components are intact, but in the absence of muscle the involved part of the diaphragm yields to pressure While this condition occurs on the right side, it is much more frequent on the left Although most authors believe it is always congenital, there are those who are of the opinion that it is sometimes acquired through injury or disease of the phrenic nerve or degeneration of the diaphragmatic muscle accompanying and following such diseases as diaphragmitis

Elevation of the diaphragm occurs about twice as often in men as in women In 1935 Reed *et al* added 2 cases to the 181 others reported in medical literature Among 412,149 military inductees, Kinzer *et al* found 35 cases on routine x ray film inspection Beeler reported 3 cases per 10,000 persons examined at the Mayo Clinic between 1938 and 1947

Nylander et al pointed out that partial eventration, that is, elevation of only a part of the diaphragm, occurs less frequently than total eventration and has been more often reported on the right side

Symptoms may be entirely absent and the diagnosis is made during an examination for some other condition or at postmortem When present, symptoms consist of dyspnea, substernal pain, discomfort or pain after meals, and occasionally nausea and vomiting In newborn infants, eventration may cause such [illegible]acks of cyanosis and severe dyspnea

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Tympany may be elicited over the lower chest when air and fluid are present in the stomach and intestines occupying the space. The gurgling sounds commonly heard over the abdomen may be elicited high over the chest. *There is no asymmetry of the chest.*

X ray inspection was first used in diagnosis in 1901 when Hirsch diagnosed hernia of the diaphragm but the postmortem examination revealed it to be a case of eventration. However since that time the x ray film has played an important role in diagnosis. It reveals an abnormally high position of the diaphragm sometimes reaching the second interspace anteriorly. Its contour is curved and regular as usual. *The diaphragm undergoes an excursion during respiration* but is definitely limited. On inspiration the mediastinum may move toward the unaffected side and the heart is usually displaced toward the normal side. *When one introduces air into the peritoneal cavity* it separates the diaphragm from the abdominal contents immediately below and thus enables one to visualize the diaphragm more distinctly. Barium introduced into the *gastrointestinal tract shows* the high position of these organs on x ray inspection.

Eventration of the diaphragm is not so uncommon but that it should be kept constantly in mind as it is important that it be diagnosed accurately. Without adequate examination the condition may be mistaken for fluid or pus in the pleural cavity and obviously the introduction of a needle may be hazardous. Pulmonary abscess, atelectasis, neoplasms and other diseases which attack the lower lobes of the lungs as well as tumors of the diaphragm, neoplasms and cysts of the liver and pericardial cysts *may be wrongly diagnosed* in a case of eventration. Differentiation between this condition and diaphragmatic hernia may be extremely difficult. Indeed exploratory laparotomy may be necessary. However it is important to make the differentiation because hernia may require surgical treatment which usually is not indicated in eventration.

Persons with eventration of the diaphragm should have the condition diagnosed so they can be warned against strenuous exercise or any activity or condition resulting in unusual abdominal pressure such as accumulation of large *quantities of abdominal fat*. Should pregnancy occur delivery is best accomplished by abdominal section as usual labor may result in rupture of the diaphragm with fatal termination.

TREATMENT

The newborn infant having episodes of *dyspnea and cyanosis from eventration of the* diaphragm requires immediate treatment. Oxygen is given continuously with the infant in the sitting position. If this results in marked decrease of symptoms surgery may be post*poned for approximately a year*. If oxygen does not relieve symptoms or if acute episodes recur immediate surgical treatment is indicated.

In most cases of eventration of the dia*phragm no treatment is necessary*. However when distressing pulmonary or gastric symptoms are present surgery may be indicated.

In recent years various surgical procedures have been employed to lower and strengthen *the diaphragm near its normal position*. These have consisted of plication by suture in as many layers as necessary. When such procedures as plication reinforcement with fascia lata suture or with tantalum mesh gauze has been employed all cases have been successful.

PARALYSIS OF THE DIAPHRAGM

Paralysis which may be unilateral or bilateral is caused by lesions involving the spinal cord or the phrenic nerve. Hemorrhage poliomyelitis and tumors of the cord are common causes and they may result in bilateral paralysis. Injuries or operations on the neck may crush or sever the phrenic nerve and thus result in temporary or permanent diaphragmatic paralysis on the same side. Birth injury may so involve the brachial plexus as to cause paralysis of the diaphragm. Disease such as tuberculosis adjacent to the phrenic nerve as

it courses through the thorax may involve it so as to result in paralysis of the diaphragm. When phrenic exeresis or evulsion was practiced in the treatment of pulmonary conditions, particularly tuberculosis, the diaphragm usually was permanently paralyzed. However when permanent paralysis, produced in this manner, was found to result in serious symptoms in some cases exeresis was abandoned for the most part and phrenemphraxis, which consists of crushing the nerve, was substituted. Following such crushing the nerves usually regenerate in 3 to 6 months after which the diaphragm again resumes its function. When the diaphragm is paralyzed from any cause for a considerable period of time, there is atrophy of the muscle and consequent weakness which may permit rupture, if undue pressure is exerted on the abdomen. It is important, therefore, that diaphragmatic paralysis be recognized and individuals warned of the possible danger.

Although Lemon and others have shown that the entire diaphragm may be paralyzed without causing dyspnea on mild exertion, severe symptoms may appear and even result fatally in cases of bilateral diaphragmatic paralysis. Excitement or even moderate exertion often results in marked dyspnea. Symptoms usually are slight or absent in cases of unilateral paralysis. However, in occasional cases severe abdominal disturbances have been reported following paralysis of the diaphragm. This is particularly true on the left side, since marked elevation may change the position of the subjacent digestive organs in an unfavorable way. Persons with extensive adhesions in the upper part of the abdomen may suffer severe symptoms, and an occasional death has been reported following interruption of the phrenic nerve. In fact, Stansbury in a group of 11 cases reported 4 deaths from gastro duodenal obstruction.

On x ray inspection the paralyzed part of the diaphragm may be as high as the third rib or second interspace anteriorly. It remains elevated during inspiration. Paradoxical movements are often observed, that is, when the uninvolved side of the diaphragm moves downward on inspiration the paralyzed side moves upward and vice versa. However, the excursion on the paralyzed side is markedly limited.

There is no *treatment* capable of restoring the function of the paralyzed diaphragm.

SPASM OF THE DIAPHRAGM

HICCOUGH (HICCUP, SINGULTUS)

Hiccough is the result of a sudden contraction of the diaphragm and the characteristic sound is produced in the larynx by the quick closure of the glottis. It is usually produced reflexly from some area of irritation within the abdomen or the thorax, such as peritonitis, typhoid fever, operations for abdominal conditions or wounds of the abdomen, gastritis resulting from alcoholic beverages, etc., distention of the stomach from over eating or gas, hyperacidity, etc. These are common causes of mild forms of hiccough. In the thorax, pleuritis or pericarditis may result in this condition. Another common cause is involvement of the phrenic nerve anywhere along its course, from the nucleus in the brain (medulla) to its terminal fibers. Tumors in the medulla, encephalitis, injuries to the nerve from wounds and trauma, pressure from tumors in the neck or chest, disease of the meninges or vertebrae in the region of the third and fourth spinal roots, alcoholic neuritis, lead poisoning involving the phrenic nerve, inflammation of the terminal fibers within the diaphragm from conditions below or above the diaphragm, such as peritonitis and pleuritis, may result in hiccough. Sometimes it is an hysterical manifestation. Hiccough is usually a sporadic condition. However, it has been reported in epidemic form when it is thought to be associated with encephalitis.

The onset is sudden regardless of the cause. There may be only a few contractions of the diaphragm, after which the condition completely disappears. Again, the contractions

may occur at the rate of 10 to 20 times per minute for approximately a day and recur after a brief period of relief When hiccough persists pain and soreness may be experienced over the attachments of the diaphragm to the chest wall Occasionally the condition may last for months

The characteristic sound makes the *diagnosis* simple However the detection of the underlying cause may be extremely difficult On fluoroscopic inspection one is able to observe the clonic spasms at approximately the same time that the characteristic sound is heard

There is no specific *treatment* The great majority of cases are of such short duration that treatment is not indicated Numerous procedures have been recommended such as drinking a glass of cold water holding the breath for 30 to 60 seconds or taking a small amount of snuff When hiccough is suspected of being on an hysterical basis anything that suddenly frightens the patient such as dashing cold water or spraying ether on the abdomen may suffice When hyperacidity is suspected one half teaspoonful of sodium bicarbonate and two or three glasses of water may quickly correct the condition Other procedures have been employed with some degree of success such as grasping the tongue and holding it in a pulled-out position for several minutes washing the stomach administration of emetics or 1 dram of Hoffman s anodyne

Inhalation of 7 to 10% carbon dioxide serves as a strong stimulant to the respiratory center In most cases however the hiccoughs stops as the individual verges on loss of consciousness and therefore cessation appears to be in part related to the generalized subsequent muscular relaxation Nikethamide in 2 to 5 cc doses introduced intramuscularly produces deep respirations and often stops the attacks

Ether in 0 5 cc doses administered subcutaneously together with carbon dioxide inhalation usually results in temporary relief However with repeated doses of ether a permanent result may be expected (the patient should be informed that subcutaneous administration of ether results in intense pain momentarily)

In persons who are highly nervous or apprehensive about the condition, sedation may be necessary One may begin with bromides in 15 grain doses If this does not suffice 5 grains of phenobarbital may be given In severe cases $^1/_6$ of even $^1/_4$ grain of morphine sulphate may be indicated

In most cases of simple hiccough there is bilateral contraction of the diaphragm However when there is involvement of the phrenic nerve the condition is usually unilateral and if it persists unduly long phrenemphraxis on the involved side may be necessary When neuritis is suspected particularly that due to alcohol large doses of vitamin B may control the condition When lead poisoning is responsible further contact with lead should be avoided

Hiccough usually is a simple and harmless condition However if it persists it may lead to exhaustion and ultimately to death When the diaphragm becomes weak from prolonged hiccough the base of the lung does not fill well with air on inspiration and congestion results The dangers of bronchitis and pneumonia are then obvious When prolonged hiccough occurs in persons suffering from terminal diseases it often indicates that death is near

Diaphragmatic *tic or spasm* has been reported following encephalitis in which the contractions occur from 60 to 200 times per minute In such cases fluoroscopic inspection of the diaphragm reveals these contractions On respiration the diaphragm is seen to descend and ascend while the small rapid contractions continue In some cases temporary or permanent interruption of the phrenic nerve has been necessary

EPIDEMIC TRANSIENT DIAPHRAGMATIC SPASM

Epidemic transient diaphragmatic spasm was first reported by Debney in 1888 While the condition resembled dengue he still considered it an independent entity By patients it was called devil s grippe" The onset was sudden with chest pain and increased respiratory rate In 1925 Payne and Armstrong reported a similar epidemic in the same state namely Virginia They found that the attack nearly always began suddenly and without

warning with severe epigastric pain which later extended to one or both sides of the lower part of the thorax Respiration was difficult, and in some cases the rate was 60 per minute From the onset the temperature rose and reached a maximum of from 101 to 105°F However, some patients experienced no fever Profuse perspiration was the rule Nausea and vomiting occurred in about one third of the patients There was no other gastro-intestinal disturbance in the beginning but in a number of cases 3 or 4 days from the onset there was diarrhea and other evidence of dysentery Headache was present in approximately one half of the patients After about 4 hours of severe paroxysms of pain and dyspnea the symptoms subsided In no case did severe symptoms persist more than 24 hours, without relief There was some recurrence of the condition, but symptoms were less mild than on the initial attack In some cases the abdominal pain was so severe and the muscles so rigid as to cause physicians to suspect acute abdominal conditions Indeed, laparotomy was done in one case but no abnormality was found The total number of leukocytes was not increased in eleven cases studied, and the neutrophiles varied from 25 to 75%. One patient developed streptococcic empyema following the initial illness In several, dysentery followed 6 days or more after the onset One physician reported 26 cases of otitis media occurring in 18 families after attacks of this condition No death was reported, except that of one woman who developed an acute endocarditis after recovery from the illness

The etiology of this condition has not been determined However, Payne and Armstrong believe it is due to an infection, the nature of which was not known In the epidemic they described, the patients were reported by 38 physicians from 22 counties, and the infection apparently spread through families by contact Among 17 families they found 5 cases in one, 4 in one, and 3 in two other families One physician reported a family in which there were ten members and all were victims within a period of about 2 weeks The epidemic was confined almost entirely to rural communities and slightly more children than adults were attacked

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CHAPTER 24

Diseases of the Esophagus

PORTER P VINSON, M D

INTRODUCTION

No PORTION of the alimentary tract is subject to the variety of lesions encountered in the esophagus However the esophagus as a site of disease is frequently overlooked and too often there is lack of understanding of efficient methods of treatment for diseases of the esophagus

Inaptitude in technical training on the part of specialists in the field of gastroenterology plus a lack of knowledge of general medicine on the part of otolaryngologists have been the greatest factors in limiting interest in and understanding of diseases of the esophagus The gastroenterologist is too prone to consider the esophagus outside his diagnostic domain and the otolaryngologist frequently limits his study of this organ to inspection through an esophagoscope With the renaissance in management of thoracic diseases interest in lesions of the esophagus is as desirable as it is inevitable

METHODS OF DIAGNOSING ESOPHAGEAL DISEASE

In diagnosing disease of the esophagus as careful an evaluation of symptoms is required as is required in detecting disease in any other part of the body A history of familial tendency to certain diseases the type of previous illnesses and operations and a thorough knowledge of the development of the present illness will indicate accurately the nature of a lesion in the esophagus in at least 90% of the cases Physical examination may reveal evidence of gradual or rapid loss of weight dehydration and physical weakness or metastatic nodules in various locations in patients with malignant lesions A smooth reddened tongue with cracks in the corners of the mouth and enlargement of the spleen indicate that prolonged dysphagia is associated with the so called Plummer Vinson syndrome, or hysterical dysphagia

Laboratory studies are less valuable as an aid in diagnosing lesions of the esophagus than in diagnosing disease in other parts of the body and because of the patient s starvation and dehydration associated diseases such as diabetes mellitus or anemia may be overlooked Severe hypochromic anemia is characteristic of hysterical dysphagia

Roentgenoscopic examination is one of the most necessary and most accurate methods of diagnosing esophageal lesions However when obstruction of the esophagus is pronounced a suspension of barium should not be ingested because swallowing this mixture may complete an otherwise partial obstruction with the result that gastrostomy may be required for feeding In patients in whom obstruction of the esophagus has resulted from impaction of a foreign body such as a bolus of meat presence of barium in the esophagus adds greatly to the difficulty of oral endoscopic visualization and to the removal of the foreign body When ingestion of a radio opaque substance is thought necessary in patients having complete or almost complete obstruction of the esophagus the use of lipiodol is preferable to a suspension of barium

Although esophagoscopic examination is a desirable and necessary procedure in the management of many lesions of the esophagus not all patients with esophageal disease require this study Esophagoscopic inspection is never an emergency procedure and should always be deferred until other examinations have been

completed When there is no contraindication to use of a general anesthetic esophagoscopic examination can be accomplished with greater safety and more comfort under general anesthesia than by employing a local anesthetic in the hypopharynx General anesthesia is especially helpful when large foreign bodies such as bones and portions of dental plates must be removed from the esophagus

FUNDAMENTAL PRINCIPLES IN MANAGEMENT OF LESIONS OF ESOPHAGUS

The esophagus is a thin musculomembranous tube and may be perforated easily by foreign bodies by lesions affecting it and by instruments used in diagnosis or treatment The first principle to be observed therefore is avoidance of unnecessary instrumentation and undue trauma in introducing instruments into the esophagus Passage of a stomach tube may result in perforation of the esophagus with accompanying mediastinitis

Esophagoscopic examination should be carried out when necessary for diagnosis and treatment of esophageal lesions but not all patients who have symptoms referable to the esophagus require direct inspection of that organ In no circumstances should unguided instruments be introduced into the esophagus In passing dilating sounds into the esophagus a previously swallowed silk thread should always be used as a guide The practice of attempting to dislodge foreign bodies in the esophagus by passing a stomach tube should be condemned Fatalities frequently follow this practice and a foreign body in the esophagus does not constitute such an emergency that drastic rapid action is justified

The second principle to be borne in mind in esophageal instrumentation is the comfort of the patient If difficulty is anticipated in introducing an esophagoscope under local anesthesia a general anesthetic should be used When local anesthesia is employed care should be taken to desensitize the hypopharynx thoroughly and the instruments should be introduced into the esophagus as gently as possible When a previously swallowed guiding thread is utilized in passing sounds into the esophagus preliminary anesthesia is not required

CARCINOMA OF ESOPHAGUS

Carcinoma of the esophagus is a common cause of dysphagia in men in women esophageal carcinoma occurs much less frequently the ratio being about 1 to 5 Although carcinoma of the esophagus has been reported in relatively young people the majority of the patients with this disease are over 40 years of age In approximately 5 to 10% of all cases of carcinoma in men the lesion is located in the esophagus whereas in only 1 or 2% of the cases of carcinoma in women is the lesion found in this organ

The most frequent and usually the earliest symptom of esophageal carcinoma is difficulty in swallowing solid food If the malignant lesion encircles the lumen of the esophagus obstruction to passage of solid food may occur relatively early in the course of the disease but if the lesion is limited to only a portion of the circumference of the tube significant symptoms may be deferred until the disease is extensive and widespread As the lumen of the esophagus is reduced in size swallowing becomes increasingly difficult and the patient is unable to retain fluids Until this degree of obstruction obtains regurgitation is seldom a predominating symptom

Pain rarely occurs until the lesion has extended beyond the confines of the esophagus but a feeling of fullness or distress may be noted when the growth is still limited to the lumen Regurgitation of blood may be noted during the course of esophageal carcinoma and fatal hemorrhage may occur in the later stages of the disease Hiccups is a frequent symptom especially when carcinoma is located near the cardiac end of the esophagus

One of the distressing complications of carcinoma of the esophagus is formation of esophagobronchial or esophagotracheal fistula

from ulceration of the growth into the air passages. When perforation occurs strangulation on swallowing liquids is noted. However, this type of lesion must be differentiated from that which is located in the upper portion of the esophagus causing obstruction and overflow of secretion through the larynx into the trachea. Esophagotracheal fistula from carcinoma developed in one of my patients within one week after onset of dysphagia which was the initial symptom.

Laboratory studies are seldom helpful in diagnosing carcinoma of the esophagus and may even be actually misleading in that anemia and cachexia which are apparently present may not be detected by laboratory examination because of dehydration and concentration of the blood.

Roentgenoscopic examination is an aid in diagnosing carcinoma of the esophagus but irregularities and filling defects that are considered characteristic of carcinoma may result from food retained in the esophagus above a benign stricture. The diagnosis of carcinoma of the esophagus is *never* justified on the basis of roentgenoscopic studies alone. In patients having pronounced or complete esophageal obstruction roentgenoscopic examination should be deferred until after esophagoscopic inspection or until a thread has been swallowed to permit passage of dilating sounds through the esophagus. Ingestion of a barium meal may *complete impending* obstruction thus necessitating gastrostomy, or it may so cover the lesion with barium that the value of direct inspection of the esophagus is reduced. Esophagoscopic examination with removal of tissue for microscopic study should be done if gastrostomy or surgical removal of the tumor is contemplated but if palliative dilation is anticipated direct inspection of the lesion is not always necessary.

TREATMENT

Treatment of patients with carcinoma of the esophagus is usually unsatisfactory and temporary relief from dysphagia is about all that can be accomplished. Dilation of the area of narrowing in the esophagus by sounds passed over a previously swallowed twisted silk thread will provide partial or complete relief from dysphagia for 6 or 8 weeks. Further stretching will frequently prolong life for 6 months or more with a fair degree of comfort.

In order to obtain relief from dilation sounds size 40 to 45 French must be passed through the malignant stricture. Dilations can be carried out with a minimal degree of discomfort and with relatively little risk if sounds are guided through the stricture over a previously swallowed silk thread. In impending perforation passage of a sound may result in mediastinitis with fatal outcome but this complication has occurred in not more than 1% of the number of my patients who have been thus treated.

Gastrostomy has been recommended frequently for palliative management of esophageal carcinoma. The immediate risk of the operation and failure to provide significant comfort or to increase length of life would indicate the futility of this procedure.

Treatment by radium and deep roentgen rays for malignant growths *in the esophagus* has proved ineffectual and has added to the discomfort of the patient when the treatment was given in sufficient amount to produce nausea and vomiting.

Operative removal of carcinoma of the esophagus has been accomplished in many instances but because of the high degree of malignancy *of such growths* recurrence usually takes place within a short time so that life is rarely prolonged. Growths located at the cardia are more amenable to surgical treatment than those in the upper or middle portion of the esophagus. Improvement in technique, the liberal use of whole blood transfusions and employment of antibiotic agents have reduced immediate mortality following surgical removal of esophageal growths but few patients survive for prolonged periods of time.

CICATRICIAL STRICTURE OF ESOPHAGUS

Any inflammatory lesion that involves the mucous membrane or muscular coats of the esophagus may narrow the lumen of the tube when healing occurs thus producing cicatricial

stenosis Difficulty in swallowing solid food usually occurs when scarring of the esophagus is severe enough to reduce the size of the lumen to 30 or 35 French

Accidental ingestion of a solution of sodium or potassium hydroxide in the form of commercial lye is the most common cause of cicatricial esophageal stricture Various types of inorganic acids and solutions of silver nitrate and formaldehyde accidentally ingested may also produce strictures of the esophagus or stomach I have observed several patients in whom cicatricial stricture of the esophagus apparently resulted from irradiation of the chest and mediastinum, following removal of carcinoma of the breast Another common cause of cicatricial stricture is the so called short esophagus type of diaphragmatic hernia Ulceration at the junction of the esophagus and hernial sac frequently occurs in these patients and stricture follows healing of the area of ulceration Excessive vomiting, such as is seen in patients with intestinal obstruction or pernicious vomiting of pregnancy, may be followed by development of esophageal stricture Diphtheria, typhoid fever and scarlet fever have also been responsible for ulceration in the esophagus, with resulting stenosis

In the majority of cases of benign stricture of the esophagus, the cause is easily ascertained and the diagnosis is seldom difficult In other instances, however, differentiation of a benign from a malignant lesion may be impossible, in which case the patient should always be treated as though he had a non malignant stricture Occasionally, malignant degeneration may occur in scar tissue in the esophagus following a burn from ingestion of lye

Roentgenoscopic examination of the esophagus usually reveals a smooth obstruction in the case of a benign stricture, but sometimes filling defects may result from small bits of food retained in the esophagus However, a smooth obstruction may also be noted with carcinoma

When the cause is apparent, esophagoscopic examination is rarely indicated for benign stricture, unless the presence of a foreign body above the area of stenosis is suspected When the cause of the stricture is not evident, esophagoscopic study may be helpful in determining the nature of the obstructing lesion

TREATMENT

Gradual dilation of cicatricial esophageal stricture will eventually result in complete and permanent relief from dysphagia When the stricture has resulted from swallowing lye, treatment will be required for approximately 2 years

Sounds should be passed through the esophagus over a previously swallowed silk thread I usually pass a size 28 or 30 French sound at the first dilation, increase the size of the sound with each treatment and extend the length of time between each succeeding dilation After three or four dilations at intervals of 1 to 2 weeks, the time between treatments can be lengthened to 3 or 4 weeks A fairly good indication for the necessity for treatment is dysphagia when the patient attempts to swallow mashed potatoes Eventually the stricture should be dilated to the size of a 45 French sound, and a lumen of this caliber should be maintained to insure permanent comfort in swallowing

Gastrostomy is rarely required in the management of benign stricture of the esophagus and when performed usually indicates neglect in treatment Complete organic occlusion of the esophagus is seldom encountered and, in most cases of benign stricture, the lumen of the esophagus can be restored and maintained by appropriate treatment

Surgical resection of benign stricture is rarely required and may be associated with formidable complications

When patients are seen immediately after ingestion of lye, stricture may be prevented by the liberal administration of antibiotic agents and cortisone

CARDIOSPASM

The most frequent cause of dysphagia in women and the second most frequent cause in men is cardiospasm The exact nature of this lesion is not thoroughly understood, and nu-

merous theories have been advanced to explain the cause of the disability

The most plausible explanation for the changes found in this disease is a disturbance in the nerve supply of the musculature of the esophagus Degenerative changes in the fibers of the vagus nerves with relative overactivity of the sympathetic innervation are probably responsible for the signs and symptoms that accompany cardiospasm Because the disease apparently results from alteration in the nerve supply of the esophagus physicians who are not familiar with such lesions may conclude that emotional factors are responsible for production of symptoms This conclusion is entirely erroneous Cardiospasm may occur at any age and is more often seen in men than in women Patients having dysphagia from cardiospasm are usually more stable emotionally than the average normal individual

The cardinal symptoms are difficulty in swallowing regurgitation epigastric pain and various symptoms related to the respiratory tract Dysphagia may begin suddenly or the onset may be gradual The feeling of obstruction is usually at the cardia or it may be located high in the esophagus At first the sensation of food sticking in the esophagus may be more or less intermittent but soon it becomes continuous and is noted at every meal although the severity of this symptom may vary Any type of food—solid soft or liquid—may give trouble and frequently the greatest difficulty is experienced in drinking cold water or carbonated beverages Apples and popcorn are especially troublesome

As difficulty in swallowing progresses regurgitation of food becomes a prominent symptom At first, food is regurgitated almost immediately following ingestion but as the esophagus becomes dilated food and secretion may be retained for hours or days and then delayed regurgitation is noted Nocturnal regurgitation and strangulation may become distressing causing loss of sleep aspiration of material into the tracheobronchial tree with resultant infection and eventually chronic bronchiectasis or pulmonary abscess Epigastric pain is experienced by 60 to 70% of the number of patients who suffer from cardiospasm This pain may be associated with swallowing and obstruction to food or it may occur independent of eating Often the pain is momentary and crampy in character or it may be severe and prolonged with location and distribution suggesting gallstone colic or coronary thrombosis Pulmonary symptoms as noted above may result from aspiration of food and secretion into the air passages or cough dyspnea and cyanosis may occur from pressure on the trachea and bronchi by a dilated esophagus filled with food

Physical examination rarely reveals any significant evidence of cardiospasm other than dehydration or starvation in those patients in whom obstruction to food or fluids has been prolonged or severe Roentgenoscopic study discloses smooth obstruction at the cardia usually associated with a moderate or great degree of dilation and sometimes with angulation of the esophagus above the point of obstruction Occasionally irregularity of the area of occlusion will be produced by food that has been retained in the esophagus Small defects in the contour of the esophagus at the cardia may suggest the presence of ulceration

Fortunately esophagoscopic examination is seldom required in diagnosing and treating patients with cardiospasm When direct inspection is made of the esophagus in such a patient much time is required in evacuating retained secretions which adds greatly to his discomfort After food and secretion have been evacuated the wall of the esophagus is frequently found to be coated with a grayish white material which resembles the coating on the tongue Ulceration is usually present especially near the cardia Sometimes there may be difficulty in locating the cardia and often the esophagoscope cannot be introduced into the stomach

TREATMENT

Treatment with drugs is usually futile although occasionally temporary relief from dysphagia may be obtained by the use of belladonna Pain may be controlled by sipping hot water Sedative drugs should never be used for relief of the pain associated with cardiospasm except for that occasioned by forcible dilatation of the cardia Treatment through

an esophagoscope for ulceration in the esophagus and use of bland diets are of no value and should not be employed with expectation of beneficial results Numerous operations have been devised and recommended for the relief of cardiospasm including resection of the stomach plastic procedures on the cardia resection of the nerve supply of the cardia and anastomosis of the esophagus with the stomach or small intestine however almost all patients who suffer from cardiospasm can be relieved completely from symptoms or improved sufficiently by dilation of the cardia to make other operative procedures unnecessary

Passage of a sound size 60 French guided over a previously swallowed silk thread into the stomach will provide complete and permanent relief for about ten per cent of the number of patients who have this disease The remaining number of patients require dilation with the Russell hydrostatic dilator before relief is obtained and one dilation of the cardia is usually sufficient to provide complete relief from dysphagia Mild recurrence of symptoms is experienced by 25% of this number however within a period of 6 months after treatment but subsequent dilation provides permanent relief for almost all those who have a return of symptoms During the past 33 years I have performed without fatality approximately 1 800 dilations for cardiospasm using the procedure as outlined above

DIFFUSE SPASM OF ESOPHAGUS AND INTERMITTENT SPASM AT CARDIA

Whereas cardiospasm is a disease independent of other intra abdominal lesions diffuse spasm of the lower half of the esophagus or mild intermittent spasm at the cardia may result from various lesions within the abdomen Often the symptoms of diffuse spasm of the esophagus cannot be distinguished from those produced by cardiospasm However in patients having diffuse spasm complete symptomatic obstruction of the esophagus occurs more frequently than in patients having cardiospasm and pain may be protracted and severe Dysphagia from intermittent spasm at the cardia is not so constant as that from cardiospasm

In diffuse esophageal spasm roentgenoscopic study reveals marked spastic contraction of the lower half of the esophagus without dilatation of the esophagus above the area of obstruction In intermittent spasm obstruction can rarely be demonstrated by roentgenoscopic examination

Treatment of patients with diffuse and intermittent spasm—particularly with the former—is less satisfactory than that of patients with cardiospasm Symptoms may persist in spite of repeated stretching of the cardia with sounds and with the Russell hydrostatic dilator As a rule as much or more relief will be obtained by passage of large sounds through the cardia than by hydrostatic dilation A careful study should be made for obscure intra abdominal lesions and when identified appropriate treatment should be instituted

CONGENITAL MALFORMATIONS OF ESOPHAGUS

Congenital abnormalities of the esophagus occur fairly frequently and vary in type from a web like diaphragm partly occluding the esophageal lumen to complete absence of the organ The most common type of abnormality consists of direct communication of the distal segment of the esophagus with the trachea or with one of the main bronchi with the proximal segment ending as a blind pouch Until recently the only type of congenital defect of the esophagus which was compatible with life was that in which the esophageal lumen was partially occluded by a web like reduplication of the mucous membrane

Dilation of the area of narrowing will restore normal deglutition and often one or two stretchings of the stricture will provide permanent relief from dysphagia In other cases

merous theories have been advanced to explain the cause of the disability.

The most plausible explanation for the changes found in this disease is a disturbance in the nerve supply of the musculature of the esophagus Degenerative changes in the fibers of the vagus nerves, with relative overactivity of the sympathetic innervation, are probably responsible for the signs and symptoms that accompany cardiospasm Because the disease apparently results from alteration in the nerve supply of the esophagus, physicians who are not familiar with such lesions may conclude that emotional factors are responsible for production of symptoms This conclusion is entirely erroneous Cardiospasm may occur at any age and is more often seen in men than in women Patients having dysphagia from cardiospasm are usually more stable emotionally than the average normal individual

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As difficulty in swallowing progresses, regurgitation of food becomes a prominent symptom At first, food is regurgitated almost immediately following ingestion, but as the esophagus becomes dilated food and secretion may be retained for hours or days, and then delayed regurgitation is noted Nocturnal regurgitation and strangulation may become distressing, causing loss of sleep, aspiration of material into the tracheobronchial tree with resultant infection, and eventually chronic bronchiectasis or pulmonary abscess Epigastric pain is experienced by 60 to 70% of the number of patients who suffer from cardiospasm This pain may be associated with swallowing and obstruction to food, or it may occur independent of eating Often the pain is momentary and crampy in character or it may be severe and prolonged, with location and distribution suggesting gallstone colic or coronary thrombosis Pulmonary symptoms as noted above may result from aspiration of food and secretion into the air passages, or cough, dyspnea and cyanosis may occur from pressure on the trachea and bronchi by a dilated esophagus filled with food

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retention of food in the sac thus established may increase the patient s discomfort Treatment consists of relieving the obstruction below the sacculation by appropriate methods This type of diverticulum is known as the traction pulsion kind

Pulsion

The third variety of sacculation of the esophagus is known as pulsion diverticulum While this kind occurs less frequently than the traction type the lesion always produces symptoms and is more easily recognized than the other varieties The true pulsion type of esophageal diverticulum occurs just above the opening into the stomach

Careful examination is required to differentiate diverticulum of the esophagus from cardiospasm from diverticulum of the cardiac portion of the stomach and from herniation of the stomach through the esophageal hiatus in the diaphragm A feeling of distress after eating regurgitation of food and difficulty in swallowing are the prominent symptoms associated with the disorder Nocturnal regurgitation may be troublesome and chronic infection of the lungs may result from repeated aspiration of material regurgitated from the esophagus during sleep Unless dilation of the cardia with sounds or hydrostatic dilator affords relief operative measures should be recommended The diverticulum may be removed or symptomatic relief may be obtained by anchoring the dependent portion of the sac at a level above the opening into the esophagus The latter procedure prevents food and secretion from entering the sac and eliminates symptoms

The most frequently recognized diverticulum associated with difficulty in swallowing is the one which forms in the lower portion of the hypopharynx just above the entrance of the esophagus Although this diverticulum is usually designated as pharyngoesophageal the term pharyngeal more accurately describes the location of the sacculation

Pharyngeal or pharyngo esophageal diverticula are usually observed in men over 40 years of age The majority of patients whom I have observed with this condition have experienced symptoms for more than 2 years At first the patient is disturbed with an increase of mucus in the throat and later with difficulty in swallowing Any type of food seems to stick in the upper portion of the esophagus and after eating small amounts of material are regurgitated Noisy deglutition soon ensues often proving a source of embarrassment if the patient is eating with strangers or in a public place Sleep may be disturbed by nocturnal regurgitation and aspiration of material retained in the diverticulum As a result of aspiration infection of the lungs may occur

Dysphagia is usually slowly progressive but when the sac attains a large size the weight of the diverticulum when filled with food may distort the opening into the esophagus to such a degree that complete obstruction occurs Loss of weight and strength result from an inadequate amount of food and from disturbed sleep

Diagnosis is usually not difficult because of the character of the symptoms the typical appearance of the lesion when examined roentgenoscopically and the noise elicited by making sudden pressure over the sac on the left side of the neck after the patient has swallowed a small amount of water

By using a previously swallowed silk thread as a guide sounds can be passed into the sac and then into the esophagus with findings characteristic of diverticulum This procedure may also be useful in passing a catheter into the esophagus for the purpose of introducing food into the stomach of a patient who has had severe obstruction and who is thereby weakened from starvation Employment of this method of feeding may obviate the necessity of gastrostomy and may be helpful in preparing patients for curative operations

Carcinoma may on rare occasions be encountered in the sac of a pharyngeal diverticulum and if this complication is suspected esophagoscopic study is indicated Esophagoscopic examination is usually more difficult of patients who have pharyngeal diverticula than of those who have other esophageal lesions The opening into the esophagus is located anterior to the sacculation and distortion of structures in this area may prevent identification of normal landmarks

repeated dilations are required to maintain the lumen of the esophagus In 1941 Levin reported a favorable result from operation on a patient with the usual congenital type of defect of the esophagus Operation had been performed 2 years previously and had consisted of gastrostomy 3 days after birth followed later by extrapleural ligation of the esophagus at the point of communication with the trachea Still later the upper segment of the esophagus was dissected free and withdrawn through an incision in the left cervical region Temporary connection was then established between the proximal portion of the esophagus and the gastrostomy by means of a rubber tube Construction of an antethoracic esophagus was proposed as a later procedure In June 1943 Haight and Towsley reported an excellent result in a similar type of case in which an end to end anastomosis of the esophageal segments was made following extrapleural ligation of the tracheo-esophageal fistula In recent years this operation has been employed with striking success Occasionally slight narrowing of the esophagus at the site of anastomosis will interfere with normal deglutition but this can be readily relieved by the passage of dilating sounds over a guiding thread through the area of construction

If favorable results are to be obtained following any type of operation in this kind of congenital deformity early diagnosis is essential Regurgitation of mucus inability to swallow strangling spells with cyanosis distention of the abdomen and roentgenoscopic evidence of air in the stomach should suggest the presence of congenital obstruction of the esophagus with esophagotracheal fistula Obstruction to passage of a small catheter in the upper portion of the esophagus or evidence of complete obstruction of the esophagus when a small amount of lipiodol is introduced through the catheter into the esophagus is usually sufficient to establish diagnosis

Barium should not be introduced into the esophagus as an aid in diagnosis because of the certainty of aspiration of the material into the tracheobronchial tree with resulting pulmonary complications When lipiodol is employed as a contrast medium it should be aspirated after roentgenoscopic study has been made Esophagoscopic examination may be helpful but should be avoided if simpler procedures prove satisfactory in establishing diagnosis

DIVERTICULA OF ESOPHAGUS

Diverticula of the esophagus are of three varieties (1) traction (2) traction pulsion and (3) pulsion

Traction

Traction diverticula are frequently observed in the esophagus at postmortem examination but are rarely detected during life Any inflammatory reaction in the mediastinum may involve the wall of the esophagus and when healing occurs a tiny sacculation may be formed by traction of scar tissue As the tissue contracts outward and upward food usually does not enter the sac thus formed and the diverticulum remains small in size Unless the sac becomes infected and ruptures into the mediastinum with formation of an abscess or perforates the bronchial or tracheal wall with development of a fistula the lesion usually exists throughout life without producing symptoms The majority of traction diverticula occur in the region of the left main bronchus and result from the healing of tuberculous lymphatic nodes located in this area One patient with painful deglutition whom I observed was found to have a tiny traction diverticulum of the esophagus in the region of the left main bronchus Dilation of the cardia provided relief from the pain on swallowing Esophagoscopic examination revealed a small area of puckering of the wall of the esophagus with a tiny projection which appeared to consist of granulation tissue When this area was removed with biopsy forceps and examined microscopically one tubercle was identified

Traction Pulsion

Occasionally obstruction of the esophagus below a traction diverticulum will make a small sacculation attain considerable size and

retention of food in the sac thus established may increase the patient's discomfort. Treatment consists of relieving the obstruction below the sacculation by appropriate methods. This type of diverticulum is known as the traction pulsion kind.

Pulsion

The third variety of sacculation of the esophagus is known as pulsion diverticulum. While this kind occurs less frequently than the traction type, the lesion always produces symptoms and is more easily recognized than the other varieties. The true pulsion type of esophageal diverticulum occurs just above the opening into the stomach.

Careful examination is required to differentiate diverticulum of the esophagus from cardiospasm, from diverticulum of the cardiac portion of the stomach and from herniation of the stomach through the esophageal hiatus in the diaphragm. A feeling of distress after eating, regurgitation of food and difficulty in swallowing are the prominent symptoms associated with the disorder. Nocturnal regurgitation may be troublesome and chronic infection of the lungs may result from repeated aspiration of material regurgitated from the esophagus during sleep. Unless dilation of the cardia with sounds or hydrostatic dilator affords relief, operative measures should be recommended. The diverticulum may be removed or symptomatic relief may be obtained by anchoring the dependent portion of the sac at a level above the opening into the esophagus. The latter procedure prevents food and secretion from entering the sac and eliminates symptoms.

The most frequently recognized diverticulum associated with difficulty in swallowing is the one which forms in the lower portion of the hypopharynx just above the entrance of the esophagus. Although this diverticulum is usually designated as pharyngoesophageal, the term pharyngeal more accurately describes the location of the sacculation.

Pharyngeal or pharyngo esophageal diverticula are usually observed in men over 40 years of age. The majority of patients whom I have observed with this condition have experienced symptoms for more than 2 years. At first the patient is disturbed with an increase of mucus in the throat and later with difficulty in swallowing. Any type of food seems to stick in the upper portion of the esophagus and after eating small amounts of material are regurgitated. Noisy deglutition soon ensues, often proving a source of embarrassment if the patient is eating with strangers or in a public place. Sleep may be disturbed by nocturnal regurgitation and aspiration of material retained in the diverticulum. As a result of aspiration, infection of the lungs may occur.

Dysphagia is usually slowly progressive, but when the sac attains a large size the weight of the diverticulum when filled with food may distort the opening into the esophagus to such a degree that complete obstruction occurs. Loss of weight and strength result from an inadequate amount of food and from disturbed sleep.

Diagnosis is usually not difficult because of the character of the symptoms, the typical appearance of the lesion when examined roentgenoscopically and the noise elicited by making sudden pressure over the sac on the left side of the neck after the patient has swallowed a small amount of water.

By using a previously swallowed silk thread as a guide, sounds can be passed into the sac and then into the esophagus with findings characteristic of diverticulum. This procedure may also be useful in passing a catheter into the esophagus for the purpose of introducing food into the stomach of a patient who has had severe obstruction and who is thereby weakened from starvation. Employment of

…en-countered in the sac of a pharyngeal diverticulum and if this complication is suspected, esophagoscopic study is indicated. Esophagoscopic examination is usually more difficult of patients who have pharyngeal diverticula than of those who have other esophageal lesions. The opening into the esophagus is located anterior to the sacculation and distortion of structures in this area may prevent identification of normal landmarks.

TREATMENT

Occasionally, passage of large sounds into the esophagus may afford partial relief from symptoms in patients who have small pharyngeal diverticula. However, when the sac is of moderate or large size, some type of operative procedure is required to correct the abnormality. Operations that have been employed successfully are removal of the sac in either a one or two stage procedure or anchoring the dependent portion of the sac above the opening into the pharynx. The latter procedure is one that can be done with a minimal amount of discomfort and risk and is useful in old or debilitated patients. Excision of the sac in a one-stage operation is the most desirable procedure and can be employed in the majority of patients.

HYSTERICAL AND FUNCTIONAL DYSPHAGIA

Hysterical dysphagia, or the so called Plummer Vinson syndrome, is characterized by hypochromic anemia and inability to swallow solid particles of food. Writers disagree as to whether changes in the mucous membrane of the mouth and esophagus associated with anemia of the hypochromic type is responsible for the dysphagia, or whether the difficulty in swallowing is a primary manifestation, with the anemia and possibly a state of vitamin deficiency the result of inadequate diet. Regardless of which conclusion is correct, the dysphagia associated with this interesting condition is hysterical in character.

The syndrome is seen only in women who are over 40 years of age. The majority are married, almost all have had their teeth removed and replaced by complete dentures, and the patients are usually of Scandinavian or English extraction. Interestingly, I have never seen a Jewish person with this disorder. Few of the patients with hysterical dysphagia lose any appreciable amount of weight, but a lemon tinted pallor of the skin, a smooth red tongue and cracks in the corners of the mouth are characteristic features of the syndrome. The appearance of the patient with this condition resembles that of the patient with myxedema or pernicious anemia. The spleen is frequently palpable or moderately enlarged.

Symptoms are limited to inability to swallow solid food and to weakness, the latter symptom depending on the degree of associated anemia. Inability to swallow solid particles of food may attain ridiculous proportions. Several of my patients have stated that they could eat most varieties of ice cream, but that they could not swallow strawberry ice cream because of the seeds. Others have had to strain out small particles of butter in buttermilk before this beverage could be swallowed. Even the tiniest pill cannot be swallowed until it is thoroughly pulverized. Symptoms have usually been present for 5 years or longer before medical aid is sought.

Anemia of the hypochromic type may be pronounced. As a rule the estimation of hemoglobin varies between 40 and 60%, but a few of my patients have had readings as low as 25%. Free hydrochloric acid is usually absent from the gastric secretion, but this is not a constant finding. Roentgenoscopic study is usually unsatisfactory because of the patient's fear of choking. Carcinoma of the upper end of the esophagus or actual interference with innervation of the muscles of deglutition may be suspected on roentgenoscopic examination.

Esophagoscopic study reveals a pale smooth mucous membrane, without evidence of stricture or infiltration. Following introduction of the esophagoscope or passage of large sounds, the patient is able to swallow all types of food without difficulty. The relief that results from passing any instrument into the esophagus has frequently led to the diagnosis of web or stricture, in the belief that actual dilation of an area of narrowing had been accomplished.

TREATMENT

As indicated above, the treatment of a patient with hysterical dysphagia consists in passing an esophagoscope or large sound through the esophagus into the stomach, with assurance that after "dilation," normal deglutition will be restored. Permanent relief from dysphagia,

recession of the spleen to normal size and restoration of a normal blood count follow treatment Symptoms rarely recur unless there is subsequent illness or emotional stress in which case passage of sounds will again provide relief

There is another type of functional dysphagia which affects both sexes and is not associated with anemia or splenic enlargement. This too depends on fear of choking and the patient will keep food or fluids in the mouth for indefinite periods of time stating that his "swallow won't work" Patients with this kind of dysphagia require constant encouragement without instrumentation of the esophagus

TRAUMATIC LESIONS OF ESOPHAGUS

The esophagus is an exceedingly delicate organ but it is well protected and is not frequently injured from external trauma Occasionally a gunshot or stab wound may cause perforation and infrequently compression of the thorax may result in rupture even without fracture of ribs The most common causes of traumatism to the esophagus however result from impaction of foreign bodies and introduction of instruments into the lumen of the esophagus for diagnostic or therapeutic purposes The majority of patients who swallow a foreign body especially a bone are instructed by solicitous friends and uninformed physicians to eat bread crusts in an attempt to force the foreign body into the stomach When the patient fails to dislodge the foreign body by this method the doctor may pass a stomach tube thus producing additional trauma if not perforation which may result fatally When bones especially if meat is attached become lodged in the esophagus the wall of the esophagus ulcerates rapidly and unless the bones are removed with great care reasonably early after ingestion they may cause perforation of the esophagus

Coin catchers probangs stomach tubes or other instruments should not be passed into the esophagus except under direct vision or when guided by a previously swallowed silk thread No instrument can be passed into the esophagus in any condition without an element of risk Therefore meticulous care should be observed in all esophageal instrumentation

Superficial ulceration of the esophagus is often encountered in the presence of a foreign body but healing occurs rapidly after the source of irritation is removed Local treatment is seldom indicated for this type of inflammatory lesion

Spontaneous perforation of the esophagus occurs infrequently but results fatally unless recognized early When the condition is correctly diagnosed within a few hours after rupture occurs operative repair of the perforation is usually followed by recovery

Perforation seldom results from properly performed dilation of strictures of the esophagus Even in dilating malignant strictures the risk of perforation is less than 1% if dilating sounds are guided beyond the area of stenosis by a thread that has been previously swallowed The most frequent evidences of perforation of the esophagus are pain fever and subcutaneous emphysema of the tissues of the neck If the lower portion of the esophagus is perforated pleuritis with effusion develops rapidly and usually occurs on the left side

Treatment

If perforation of a normal or recently infected esophagus can be detected immediately the area of injury should be explored provided a competent thoracic surgeon is available If there is uncertainty as to whether perforation is present or if expert surgical aid is not available expectant treatment is indicated

Within 6 months I have observed perforation of the esophagus in two patients In one patient perforation from a swallowed chicken bone was recognized immediately and surgical repair of the esophagus was followed by prompt recovery In the other patient rupture followed dilation of a cicatricial stricture of many years duration Definite evidence of

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perforation was not apparent until 12 hours after injury, and expectant treatment with liberal use of sulfonamides resulted in recovery of this patient also When perforation of the esophagus is suspected and medical rather than surgical measures are employed, no food should be given by mouth The liberal use of antibiotics as well as powdered sulfanilamide or other sulfonamides should be given orally, for local as well as for systemic effect Small amounts of water may be swallowed without increasing the risk of leakage. If improvement is apparent, orange juice and broth may be swallowed after 3 or 4 days A normal diet may then be resumed with caution

VARICES OF ESOPHAGUS

Cirrhotic changes in the liver are often associated with varices in the lower half or lower two-thirds of the esophagus, although occasionally varices may be present without demonstrable hepatic disease Usually the first manifestation of esophageal varices is vomiting of blood Hemorrhage may be severe and is frequently fatal

At times, dilated veins can be demonstrated by careful roentgenoscopic examination When this examination does not reveal the presence of varices, esophagoscopic study should be done In many cases, enlarged veins can be detected during life by direct inspection of the esophagus, when roentgenoscopic examination does not disclose any abnormality or when venous enlargement cannot be demonstrated at postmortem examination Esophagoscopic examination usually reveals evidence of ulceration in the esophagus, in addition to the bluish-colored engorged veins

Treatment of esophageal varices is usually unsatisfactory and eventually massive fatal bleeding occurs Injection of the veins with some type of sclerosing solution through the esophagoscope or directly at operation has been employed with questionable beneficial results Splenectomy and various types of operations designed to reduce the blood supply and venous pressure in the liver have been equally ineffective in controlling bleeding. Temporary control of bleeding by introducing an inflatable rubber balloon into the esophagus has been recorded Transthoracic ligation of enlarged veins in the esophagus and in the cardiac end of the stomach seems the most logical surgical approach to palliative treatment Unfortunately the condition is of constitutional origin and treatment of symptoms is about all that can be offered to patients having this abnormality

Within the past few years I have recommended to patients with esophageal varices and associated hemorrhage, the use of about a half teaspoonful or less of powdered sulfanilamide once or twice a week, on retiring at night The powder is taken without water so that prolonged local action of the drug may be obtained in the esophagus This type of therapy has apparently been effective in controlling ulceration and bleeding in several patients

UNUSUAL TUMORS OF ESOPHAGUS

Although the majority of tumors that involve the esophagus are carcinoma, benign or rare types of malignant tumors are occasionally encountered Benign tumors often attain very large size within the lumen of the esophagus without producing significant symptoms Intraluminal tumors are usually pedunculated and may be regurgitated through the mouth

Almost all varieties of benign tumor have been observed in the esophagus, those most frequently reported being polyps, myomas and lipomas Hemangiomas, adenomas and papillomas occur less often Unusual malignant tumors are sarcomas of various types and hemangio endotheliomas Exceptionally large filling defects in the esophagus, observed on roentgenoscopic examination, with indefinite and usually mild symptoms, should suggest the presence of benign tumor Esophagoscopic inspection is required for exact diagnosis

Treatment for benign tumor depends on the size and character of the lesion and on the severity of clinical symptoms Electrocoagulation through an esophagoscope may be indicated for certain types of tumors whereas removal by snare or external esophagotomy may be indicated for others

SPECIFIC INFLAMMATORY LESIONS OF ESOPHAGUS

ACTINOMYCOSIS AND BLASTOMYCOSIS

Actinomycosis and blastomycosis are rarely encountered as primary lesions in the esophagus In one of my patients with generalized actinomycosis of 28 years duration esophagotracheal fistula developed during the course of the disease The lesion in the esophagus was presumably the result of invasion of Actinomyces Another patient had a primary lesion in the esophagus which apparently resulted from blastomycosis

SYPHILIS

Syphilis probably involves the esophagus often during the secondary stage of the disease but it does not produce symptoms Stricture of the esophagus from syphilis has been reported but it is quite rare When dysphagia develops in a patient who has syphilis other causes for the difficulty should not be overlooked

DIPHTHERIA AND SCARLET FEVER

I have observed several patients with stricture of the esophagus which followed diphtheria and scarlet fever The esophagus is probably involved more frequently in these diseases than is generally supposed but permanent changes seldom result

TUBERCULOSIS

Prior to the advent of anti tuberculosis drugs difficulty in swallowing in patients having pulmonary tuberculosis was a frequent and serious complication Ulceration in the mouth and hypo pharynx and especially involvement of the epiglottis caused pain on swallowing thereby interfering with nutrition At the present time ulcerating tuberculous lesions are seldom seen in these areas and when they occur response to drug therapy is prompt

NONSPECIFIC INFLAMMATORY LESIONS OF ESOPHAGUS

Nonspecific inflammatory lesions are found in the esophagus in 7% of all patients who are examined postmortem In 10% of this number of patients symptoms referable to the esophagus had been noted but few of them had been diagnosed during life as having esophageal disease

Three types of esophagitis are frequently observed (1) acute ulcerative (2) subacute ulcerative and (3) chronic The first type is the one that is most often encountered So called peptic ulcer of the esophagus is the result of acute or subacute inflammatory reaction and is usually observed at the junction of the esophagus and upper loculus of stomach in congenital shortening of the esophagus with herniation of the stomach through the esophageal hiatus in the diaphragm Prolonged vomiting and introduction of tubes through the esophagus into the stomach for lavage or feeding are the chief causes of esophagitis I observed one patient with extensive esophagitis associated with severe diabetes mellitus

Other causes of esophagitis are infected tonsils and teeth and disease in the gallbladder or appendix Relaxation of the cardia during anesthesia with regurgitation of gastric secretion into the lower portion of the esophagus may also be a causative factor

The chief symptoms of acute or subacute esophagitis are pain hemorrhage and dysphagia The pain is located substernally and is a burning type that is not relieved by food or alkalies as a matter of fact eating intensifies

the discomfort If ulceration is sufficiently extensive scar tissue may contract the lumen of the esophagus when healing occurs and then obstruction to food is noted Bleeding may occur in small or large amounts At times dark brownish material is vomited from the stomach This material represents slow seepage of blood that has passed into the stomach and after being changed by gastric secretion is regurgitated

Unless stricture has occurred roentgenoscopic examination does not disclose evidence of esophagitis Inflammatory changes are easily discernible at esophagoscopic inspection but such examination may increase discomfort in the acute stage of inflammation and for this reason may be contraindicated

TREATMENT

Sedation for pain avoidance of esophageal instrumentation, bland diet and use of tincture of belladonna to allay spasm are the chief indications in the acute stage of esophagitis If stricture develops as healing occurs dilation will be required to restore and maintain the lumen of the esophagus Gastrostomy has been employed to provide rest for the esophagus and to facilitate healing

FOREIGN BODIES IN ESOPHAGUS AND STOMACH

Although the presence of foreign bodies in the esophagus has been widely publicized in not more than 5 to 10% of the number of patients who complain of symptoms referable to the esophagus is a foreign body the cause of the distress However foreign bodies in the esophagus usually produce serious consequences and early recognition and removal are imperative if fatalities are to be avoided

Foreign bodies are encountered in the esophagus of adults more frequently than in children In adults the foreign body usually consists of meat or bones from chicken wild game or meat chops in children open safety pins coins and other disc shaped articles are most commonly observed Occasionally a previously existing stricture in the esophagus may be responsible for lodgment of a small foreign body such as an orange seed or a small fragment of meat Stricture or localized spasm associated with congenital shortening of the esophagus and diaphragmatic hernia is often complicated by impaction of a foreign body Usually however, a foreign body becomes obstructed in a normal esophagus

Carelessness in permitting children to put coins safety pins and buttons in the mouth is responsible for their getting foreign bodies lodged in the esophagus In adults the replacement of teeth with partial or complete dentures not only interferes with mastication but reduces normal sensation in the mouth and thus causes ingestion of bones and inadequately masticated meat which may lodge in the esophagus

Although foreign bodies may become obstructed in any portion of the esophagus the most frequent point of lodgment is just below the cricopharyngeus muscle Bones in this area can usually be demonstrated on roentgenoscopic study if lateral exposure is made Anteroposterior films made of this area will reveal metallic foreign bodies but never a bone Below this area bones cannot be demonstrated directly by roentgenoscopic examination although indirect evidence of the presence of a bone or other foreign body may be obtained by observing roentgenoscopically the passage of a small amount of ingested lipiodol through the esophagus Barium in suspension should never be used for this purpose for if a foreign body is demonstrated and esophagoscopic examination is performed the presence of the contrast mixture will interfere with the inspection

Pins needles and straight fish bones are seldom found in the esophagus If they are not detected on examination of the tonsillar areas the base of the tongue or the pyriform fossae they have probably passed into the stomach Esophagoscopic study should always be done when the presence of a foreign body is sus

pected in the esophagus Ordinarily the foreign body can be removed safely through an esophagoscope. Esophagoscopic examination can usually be made using local anesthesia but when the presence of a large foreign body is suspected or there is fear of penetration of the wall of the esophagus the use of general anesthesia is preferable Intravenous injection of pentothal sodium in combination with curare is the safest and most satisfactory type of anesthetic for esophagoscopic study The introduction of an intratracheal tube prevents aspiration from the esophagus during the examination and facilitates adequate pulmonary ventilation For children I usually prefer inhalation anesthesia in removing a foreign body from the esophagus

Whenever there is difficulty in removing a foreign body such as an open safety pin from the esophagus the foreign body should be carefully pushed into the stomach Almost all foreign bodies that enter the stomach will pass through the gastrointestinal tract and be expelled spontaneously Laparotomy for removal of a foreign body from the stomach or intestines should be postponed indefinitely unless there is evidence of perforation or unless the size and position of the object make spontaneous expulsion unlikely While a foreign body such as an open safety pin is in the gastrointestinal tract laxatives should not be given The usual diet should be maintained Swallowing bread crusts in an effort to push foreign bodies from the esophagus into the stomach should be condemned

FISTULA FROM ESOPHAGUS INTO AIR PASSAGES

The most frequent cause of a fistulous opening from the esophagus into the air passages is carcinoma A malignant growth beginning in the esophagus especially if the lesion involves the anterior wall may cause perforation of the trachea or of the left main bronchus with formation of a fistula Congenital deformities of the esophagus may be associated with fistulous communications with the trachea or with one of the major bronchi Traction diverticula of the esophagus may penetrate the wall of the left main bronchus with resulting fistula Other causes for esophagotracheal or esophagobronchial fistula are tuberculosis syphilis actinomycosis or ulceration from a foreign body in the esophagus or air passages Perforation of the esophagus following intraesophageal instrumentation may also result in fistula

Symptoms from a fistula from the esophagus into the air passages depend on the cause of the perforation and on the size of the opening The most prominent symptom in any case is strangulation on swallowing liquids In patients in whom carcinoma is the cause of perforation a period of progressive difficulty in swallowing usually precedes onset of strangulation In one of my patients there was an interval of a week only from the onset of difficulty of swallowing solid food until clinical and roentgenoscopic evidence of perforation was noted

In congenital defect of the esophagus with associated fistula strangulation may be noted from overflow of an upper esophageal pouch into the larynx and trachea or the upper segment of the esophagus may communicate with the trachea and strangling may result from passage of fluid directly into the air passages Sometimes the opening into the respiratory tract may be very small thus permitting the patient to lead a fairly comfortable life In other instances chronic pulmonary infection may result from continuous leakage from the esophagus into the air passages In one of my patients with fistula strangulation could often be avoided by his eating solid food before drinking fluids Apparently the fistulous opening became occluded temporarily by solid particles of food preventing escape of fluid from the esophagus into the bronchus

When fistula is suspected careful roentgenoscopic examination using lipiodol instead of barium as a contrast medium will reveal the perforation if one exists In patients who have carcinoma high in the esophagus or in those in whom difficulty in swallowing results from interference in the nerve supply of the muscles

of deglutition overflow of fluid into the larynx may suggest the presence of fistula. Careful roentgenoscopic study is required in such cases to differentiate aspiration through the larynx from leakage through a fistula.

TREATMENT

The treatment of patients with fistula from the esophagus into the air passages depends on the cause of the opening. In patients having congenital abnormalities operation may prove successful. When the fistula has resulted from a malignant lesion no treatment will prove of very much value. Daily intravenous injection of fluid may increase comfort and prolong life. Gastrostomy seldom provides palliation. When the fistula has resulted from a nonmalignant nonspecific inflammatory lesion operation may result in successful closing of the opening. Clerf, Cooley and O'Keefe reported successful closure of fistula of this type by application of beads of sodium hydroxide into the lumen of the fistula through the esophagoscope. Formation of scar tissue effectually closed the fistulous opening.

HERNIATION OF STOMACH THROUGH ESOPHAGUS HIATUS IN DIAPHRAGM

Two types of hernia through the esophageal hiatus in the diaphragm frequently produce dysphagia. In one type the esophagus is of normal length and a portion of the stomach protrudes through the esophageal diaphragmatic hiatus into the thorax. The herniated portion of the stomach may be large or small, and the severity of symptoms is not related to the size of the hernia. Dysphagia with this kind of hernia may result from spasm of the lower end of the esophagus, from pressure from the hernial sac or from actual cicatricial stricture which is apparently related to the hernia.

In the second type of hernia the esophagus appears shorter than normal, the junction of the esophagus and the stomach being about two inches above the diaphragm. Difficulty in swallowing is a prominent symptom caused by spasm at the junction of the esophagus and stomach or by cicatricial stricture which follows the healing of ulceration at this area.

Congenital malformation is considered the cause of both types of hernia in this locality and the kind associated with apparent shortening of the esophagus is frequently termed "congenital shortening of esophagus with diaphragmatic hernia" or "sliding" hiatal hernia. Possibly shortening of the esophagus occurs in some patients as the result of longitudinal contraction associated with healing of scar tissue. I have observed four patients with this type of hernia who also had advanced scleroderma. In three of them cicatricial stricture was present, indicating that probably contraction of the esophagus had pulled a portion of the stomach into the thorax.

Almost all patients with the short esophagus or sliding type of hernia can be relieved of symptoms by passing dilating sounds into the stomach. When spasm is responsible for dysphagia, passage of a sound size 60 French will usually give prompt and permanent relief from difficulty in swallowing. When stricture is present, more frequent passage of smaller sounds may be required to restore and maintain a satisfactory lumen through the esophagus.

In the para-esophageal type of diaphragmatic hernia operative repair is often indicated and the results of operation are satisfactory. Relief from dysphagia may be obtained by passing dilating sounds into the stomach. The esophagus should always be investigated thoroughly before operation is undertaken. Operation is seldom indicated in the "sliding" type of hernia.

EXTRA-ESOPHAGEAL LESIONS CAUSING DYSPHAGIA

Difficulty in swallowing frequently results from interference in innervation of the constrictor muscles of the pharynx. Myasthenia gravis and degenerative changes in the nerve

supply of the pharyngeal muscles which may be caused by inflammatory lesions metastasis of malignant tumors or trauma may produce dysphagia Not infrequently injury to a recurrent laryngeal nerve during thyroidectomy may cause difficulty in swallowing In all patients in whom disturbance in the nerve supply of the muscles of deglutition is responsible for dysphagia the chief difficulty in swallowing is experienced with liquids Solid food may be swallowed with very little trouble but when an effort is made to swallow fluids strangulation occurs and there is regurgitation through the nose

When dysphagia becomes pronounced in a patient suffering from altered function of the muscles of deglutition a small tube can be passed into the stomach for feeding Care must be taken however that the tube is in the esophagus and not in the trachea before food is introduced

Ulcerating lesions in the mouth and pharynx may produce pain on swallowing, and tumors of the mouth, tongue and hypopharynx may interfere with deglutition Tumors of the mediastinum seldom compress the esophagus and thus cause dysphagia although occasionally an aneurysm of the aorta or an enlarged heart may make swallowing difficult Exostosis of the spine Pott's disease of the thoracic vertebrae and other spinal deformities have been reported as causes of dysphagia

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of deglutition, overflow of fluid into the larynx may suggest the presence of fistula Careful roentgenoscopic study is required in such cases to differentiate aspiration through the larynx from leakage through a fistula

TREATMENT

The *treatment of patients with fistula from the esophagus into the air passages depends* on the cause of the opening In patients having congenital abnormalities, operation may prove successful When the fistula has resulted from a malignant lesion no treatment will *prove of very much value Daily intravenous injection of fluid may increase comfort* and prolong life Gastrostomy seldom provides palliation When the fistula has resulted from a nonmalignant nonspecific inflammatory lesion, operation may result in successful closing of the opening Clerf, Cooley and O'Keefe reported successful closure of fistula of this type by application of beads of sodium hydroxide into the lumen of the fistula through the esophagoscope *Formation of scar tissue* effectually closed the fistulous opening

HERNIATION OF STOMACH THROUGH ESOPHAGUS HIATUS IN DIAPHRAGM

Two types of hernia through the esophageal hiatus in the diaphragm frequently produce dysphagia In *one type, the esophagus is of* normal length and a portion of the stomach *protrudes through the esophageal diaphragmatic* hiatus into the thorax The herniated portion of the stomach may be large or small, and the *severity of symptoms is not related to* the size of the hernia Dysphagia with this kind of hernia may result from spasm of the lower *end of the esophagus, from pressure from* the hernial sac or from actual cicatricial stricture, which is apparently related to the hernia

In the second type of hernia, the esophagus appears shorter than normal the junction of the esophagus and the *stomach being about* two inches above the diaphragm Difficulty in swallowing is a prominent symptom caused by *spasm at the junction of the esophagus and* stomach or by cicatricial stricture which follows the healing *of ulceration at this area*

Congenital malformation is considered the cause of both types *of hernia in this locality,* and the kind associated with apparent shortening *of the esophagus is frequently termed* "congenital shortening of esophagus with diaphragmatic hernia," or "sliding" hiatal hernia Possibly shortening of the esophagus occurs in some patients as the result of longitudinal *contraction associated with healing of scar* tissue I have observed four patients with this type *of hernia who also had advanced sclero*derma In three of them, cicatricial stricture was present, indicating that probably contrac*tion of the esophagus had pulled a portion of* the stomach into the thorax

Almost all patients with the short esophagus or *sliding type of hernia can be relieved of* symptoms by passing dilating sounds into the stomach When spasm is responsible for dysphagia, passage of a sound size 60 French will usually give prompt and permanent relief from difficulty in swallowing When stricture is present, more frequent passage of smaller sounds may be required to restore and maintain a satisfactory lumen through the esophagus

In the para-esophageal type of diaphragmatic hernia, operative repair is often indicated and the results of operation are satisfactory Relief *from dysphagia may* be obtained by passing dilating sounds into the stomach The esophagus should always be investigated thor*oughly before operation is undertaken* Operation is seldom indicated in the "sliding" type of hernia

EXTRA-ESOPHAGEAL LESIONS CAUSING DYSPHAGIA

Difficulty in swallowing frequently results from interference in innervation of the constrictor muscles of the pharynx Myasthenia gravis and degenerative changes in the nerve

supply of the pharyngeal muscles which may be caused by inflammatory lesions metastasis of malignant tumors or trauma may produce dysphagia Not infrequently injury to a recurrent laryngeal nerve during thyroidectomy may cause difficulty in swallowing In all patients in whom disturbance in the nerve supply of the muscles of deglutition is responsible for dysphagia the chief difficulty in swallowing is experienced with liquids Solid food may be swallowed with very little trouble but when an effort is made to swallow fluids strangulation occurs and there is regurgitation through the nose

When dysphagia becomes pronounced in a patient suffering from altered function of the muscles of deglutition a small tube can be passed into the stomach for feeding Care must be taken however that the tube is in the esophagus and not in the trachea before food is introduced

Ulcerating lesions in the mouth and pharynx may produce pain on swallowing and tumors of the mouth tongue and hypopharynx may interfere with deglutition Tumors of the mediastinum seldom compress the esophagus and thus cause dysphagia although occasionally an aneurysm of the aorta or an enlarged heart may make swallowing difficult Exostosis of the spine Pott s disease of the thoracic vertebrae and other spinal deformities have been reported as causes of dysphagia

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PART II

DISEASES OF THE CARDIOVASCULAR SYSTEM

CHAPTER 25

Physical Examination of the Heart and Great Vessels

RAYMOND F. SHEETS, M.D.

MATURE experience with the newer methods of cardiac diagnosis such as angiocardiography and cardiac catheterization has brought the realization that the physical examination is still the most important aspect of cardiac evaluation. Mitral stenosis is a condition which illustrates this point. Hence not one or all the laboratory tests is equal in importance to physical examination. It is by this procedure, along with the evaluation of the patient's symptoms, that the clinician must decide whether or not the patient has mitral valve disease and whether there is any likelihood of correction by the surgeon. Because of this one fact alone, the teaching of physical diagnosis has been rejuvenated in many medical schools and in postgraduate exercises for clinicians.

Ofttimes in medical schools the teaching of physical examination is relegated to less experienced physicians, when this discipline above all others must be taught well to be worthwhile. Often it is dull to the student when it should be stimulating. It is the student's introduction[1] to the care of patients. An informed and experienced teacher has a tremendous opportunity to teach practiced methods of collecting clinical data by use of the senses, to correlate physiologic observations with clinical problems, and to set the pattern for further clinical development of the student.

GENERAL INSPECTION

The sequence with which one proceeds to examine the chest and its contents is relatively unimportant, but it is important that the examiner develop his own system and proceed in the same manner each time. Unless this is done, the chances are very good that important parts of the examination will be omitted. The examining physician should have his own routine for all phases of the physical examination. Ordinarily in this day of medical practice, the patient is lying down either on an examining table in an office or in a hospital bed. The patient should be undressed and covered with a sheet. At first glance one can see if the patient is orthopneic and more comfortable with the head elevated. Cyanosis of the lips and distention of the neck veins may be observed. Scrutiny of the nails may be carried out for evidence of cyanosis, capillary pulsations, or clubbing. The skin may be inspected for vascular abnormalities, pigmentation, and turgor. Abnormal sweating or dryness may be observed.

General inspection permits evaluation of precordial overactivity. One should attempt to detect activity over the apical region in contradistinction to activity transmitted from the conus area. In aortic insufficiency, the apex beat ordinarily is small and localized in the sixth interspace rather than in the normal position of the fifth. A large diffuse apical beat with a slowly heaving precordium suggests hypertrophied ventricular muscle working against a stenotic aortic valve. At times it is difficult to determine whether precordial activity originates from enlargement of the

left ventricle or the right ventricle or both

The adhesions of constrictive pericarditis sometimes draw in the posterior chest wall in the region of the eleventh and twelfth ribs with systolic contraction of the heart This is Broadbent s sign Another similar phenomenon which may be striking is retraction of the ribs *overlying the apex of the heart* Care must be taken not to confuse either of these signs with the intercostal retraction which occurs normally

In general inspection of the cardiovascular system one must remember to use the ophthalmoscope which can give the examiner the only direct look at the patient s blood vessels Although this is a small sample of vessels evidence for sclerosis of the arteries or spasm may be obtained

The neck veins may be examined for pulsation and increased pressure as well as for *hepatojugular*[2] *reflux* *Firm pressure over the* edge of the liver for a minute will increase the venous pressure in the jugular vein if the liver is congested because of a failing heart Care must be taken that the patient continues to breathe normally or the hepatojugular reflux test will be invalid Normal venous pressure measured in a large antecubital vein is 8 to *10 cm of water* *The pressure here is slightly* higher than in the right auricle Elevation of venous pressure is an important sign of congestive heart failure Normally the jugular veins are collapsed with the patient sitting and filled with him lying flat A crude but valuable clinical estimation of the venous pressure may be made by gradually cranking up the head of the bed *The point of elevation at* which the summit of the column of blood in the jugular lies midway the neck provides clear evidence of increased or normal pressure

With the head of the column of blood mid way up the neck identification of jugular pulsation and transmitted carotid artery pulsation is possible Carotid pulsations push the jugular vein perpendicularly from the cervical spine Venous pulsations move the blood along the long axis of the vein Occasionally venous pulsations may be felt ordinarily not Pulsation in the jugular veins is a sign of tricuspid valve *incompetence* *This* may be corroborated by finding an expansile pulsation of the liver, but care must be taken to differentiate this from pulsation transmitted from the aorta

In an occasional normal person a humming kind of noise can be heard over the jugular vein Sometimes it is transmitted widely in *the clavicular area* *Temporary digital pres*sure in the jugular vein or even a change in position of the head and neck cause it to disappear It is caused by blood flowing through the vein and does not signify disease Venous hums also occur *occasionally in* dilated veins of the abdominal wall associated with cirrhosis of the liver

Obstruction of the superior vena cava may be detected by signs of increased venous pres*sure in the upper part of the body* Venous congestion is visible in the jugular veins and veins of the arms as well as the small superficial veins of the skin These are dilated and congested Swelling of the neck and arms is *present in addition to cyanosis of the skin*

PALPATION

Palpation is the best clinical method of determining the amount of work the heart is performing and herein lies its greatest importance *in the examination* of the heart Of course certain loud murmurs may be elicited by palpation as thrills but this method is secondary to auscultation Palpation *in fact* the entire physical examination must be performed so that both patient and examiner are comfortable Satisfactory palpation can only be done when the muscles of the examiner s hand and arm are relaxed

As the ventricles contract the left ventricle (Fig 1) rotates to the right and hits the chest wall A big active left ventricle will hit harder than a normal sized one A flabby one causes *less heaving* *By placing* the hand firmly over the apex of the left ventricle the amount of force which is felt may give insight into how much work *the left ventricle is performing*

Likewise by placing the hand over the area to the left of the sternum in the fourth interspace, one can make a useful estimation of the action of the right ventricle. In this examination it is necessary to consider the age of the patient, the configuration of the chest and the amount of emphysema if it is present. Normally in children and young women there is much more activity over the conus area than can be detected in older people and in men. The amount of overactivity present in children and young women would definitely be abnormal if it were present in an older person or a man. Thin chested individuals with little muscular covering of the thorax certainly have more activity on palpation than do heavy chested muscular persons. If a lot of emphysematous lung lies between the heart and chest wall much damping of activity will occur. These subtleties must be considered by the examiner and become part of his experience.

Contours of arterial pulses determined at the bedside, as well as pulse rates, may be a valuable aid in diagnosis. Such information may help to determine the functional significance of certain valve lesions, such as stenosis or insufficiency of the aortic valve. The noise made by a valvular deformity is not important. The important consideration is the hemodynamic alteration produced by the lesion. The contour of the arterial pulse wave may be estimated at the bedside as follows. The examiner comfortably holds the patient's arm extended with his left hand to straighten the vessels and allow a full flow of blood from the aorta. The patient's forearm is grasped firmly with the examiner's right hand. The force of the grip is gradually adjusted until the pulse is clearly felt. Palpation with the whole hand permits clearer interpretation than palpation of the radial pulse with the fingertips. A collar pulse is present when the blood pressure rises and falls away suddenly as in hemodynamically significant aortic insufficiency except infrequently when it is obscured by aortic stenosis. Other signs of aortic valve incompetence, such as Corrigan's pulse, Duroziez's sign and capillary pulse, are rarer in slight degrees of insufficiency. The

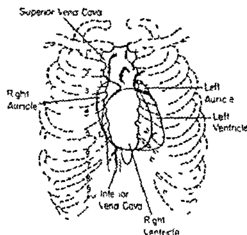


Fig. 1. In the frontal view the right border of the heart is made of segments of superior vena cava, *right auricle and inferior vena cava. The left border is mostly left ventricle except for a small segment of left auricle.* The right ventricle is covered by the sternum. The right border of a normal heart does not extend far enough beyond the sternal margin to be detected by percussion.

plateau pulse of aortic stenosis results from prolongation of the systolic ejection time of the left ventricle. Mitral stenosis causes a pulse of small volume by limiting the stroke volume of the left ventricle. In combined valve disease pulse contours may be too confusing to help in diagnosis.

The femoral arteries should be palpated routinely in the examination of all patients. It is by this method that coarctation of the aorta may occasionally be suspected or otherwise missed. When sudden occlusion of a peripheral artery of the leg occurs *it is very helpful to know that this artery was patent because the finding was so recorded on a previous physical examination. Sometimes peripheral pulses are absent as a normal variant and unless one knows whether or not they were present on a prior occasion he may be misled.*

When an abnormality of the femoral pulse is detected both iliac arteries and the abdominal aorta should be felt to determine the level of obstruction. This may be caused by dissecting aneurysm or thrombosis of the aorta. X-ray aortography can accurately de-

tect the level of aortic obstruction Prominent pulsations, caused by buckling of the common carotid, are sometimes seen or felt in the sternal notch when tortosity or lengthening of the aorta occurs

PERCUSSION

Most clinicians are familiar with the indirect method of percussion in which the tip of the middle finger of one hand is used to tap the *first joint of the middle finger of the other* hand This is the classical method and the only one usually taught in courses in physical examination One should remember to begin percussion far outside the border of the heart in order to move from an area of resonance to dullness This will permit more accurate identification of the cardiac outline

Although indirect percussion is probably the most common method taught, the direct method of percussion is more useful in determining the cardiac borders *Only a little* practice is necessary for one to learn to relax the wrist and middle finger enough to permit a sharp tap of the chest with the ball of the finger This method of percussion produces a clearer outline of the heart especially in the area of relative cardiac dullness With practice, one learns to identify the border more *by feeling the change in vibration than by* hearing the sound Percussion continues to be a useful method of clinical examination in spite of its obvious limitations Gross changes in cardiac size are detectable by percussion and no more should be expected

AUSCULTATION

Although a presumptive diagnosis of the *type of structural heart disease may be made* by the visual and tactile senses, auscultation confirms the diagnosis In certain instances, auscultation offers the only clear evidence of a particular structural defect

The type of stethoscope used is an important consideration It must be an accoustically sound instrument in order to provide true *reproduction of sounds* as well as to pick up certain noises within the heart *Some popu* lar instruments on the market are hopelessly ineffective The pickup should be a combination of diaphragm and bell of an accoustically sound design The rubber tubes connecting the ear pieces and the pickup device must be thick-walled with a fairly small lumen The *ear pieces must* fit the ears of the examiner so that good air-tight contact is obtained without discomfort The physician must have both a diaphragm and bell instrument *conveniently* available or a combination thereof because certain high pitched murmurs, such as the diastolic murmur of aortic insufficiency, can at times be heard only with the diaphragm *On the other* hand certain presystolic or diastolic murmurs at the apex can be heard better with the bell type stethoscope Unless the physician learns to use both components of this instrument competently, an unnecessary handicap is imposed on his diagnostic acumen

Differentiation of the first and second heart sounds is easy when the heart rate is slow Diastole is longer than systole and the sounds have distinct characteristics As the heart rate increases, the sounds tend to become similar Palpation of the radial pulse with the *examiner's free hand will result in confusion* because of the lag before the systolic impulse reaches it *Ordinarily, the examiner may* recognize diastolic or systolic timing by the auditory characteristics of sounds and murmurs This is not always possible and the timing should be checked at some point during auscultation by palpating the carotid artery with the thumb of the left hand

Many theories have been proposed to ex*plain the production of the heart sounds* The details are still unclear but there no longer is doubt that they are caused in large part by the heart valves *Smith, Essex, and Baldes*[3] found that most of the systolic noise in perfused hearts depends on the integrity of the mitral and tricuspid valves The second heart

sound depended on the integrity of the semilunar valves. Splitting of the first heart sound may be explained by asynchronous closure of the tricuspid and mitral valves. Asynchronous closure of the semilunar valves can explain the split second sound. This is occasionally heard in left bundle branch block. The split first sound may suggest a systolic gallop rhythm. The ominous gallop occurs in diastole and clearly resembles the rhythm produced by a galloping horse. It is associated with severe heart disease.

The middiastolic rumble and presystolic murmurs of mitral stenosis usually are heard best in the fourth or fifth interspace slightly lateral to the apex beat. On certain occasions though they may be heard best medial to the midclavicular line. Accentuation of the diastolic murmurs of mitral stenosis may be produced by increasing the heart rate with exercise or by listening for the murmurs with the patient lying in the left lateral decubitus position. Occasionally it is helpful to listen while the patient holds his breath in expiration. These maneuvers increase the intensity of murmurs by placing the heart closer to the anterior chest wall. Often the murmurs of mitral stenosis are extremely difficult to find and in a cursory examination may be completely missed. Herein lies the greatest importance in palpation and percussion since these methods of examination may offer a hint that an abnormality of the heart exists. A careful auscultatory examination may then detect crucial signs of disease.

THE ARTERIAL BLOOD PRESSURE

The arterial blood pressure should be taken during the examination at a time convenient for the examiner. The patient may be sitting or lying. In many people the first blood pressure reading will be a few mm Hg higher than a determination after the patient is relaxed. The blood pressure cuff should be placed smoothly and snugly on the arm. The arm muscles must be relaxed or the reading may be falsely elevated. As pressure in the cuff is increased the radial artery should be palpated to determine the point of obliteration of its pulse. This lends assurance to the accuracy of the systolic pressure. If the palpatory reading is different than the auscultatory method the pressure is increased about 25 mm above the point when the radial pulse is lost and then deflated slowly until the first sound is heard. The higher value is the systolic pressure. As the cuff is deflated further a change in quality of sounds may occur or the sounds may disappear entirely. If the points of change in sound and total disappearance are different both should be recorded as for instance 160/100/84.

In certain patients with hypertension there is a gap in the sounds below the true systolic pressure where they disappear abruptly only to reappear at a lower level. This is the auscultatory gap. If the cuff is inflated only to this level initially the systolic reading obtained may be erroneously low by 30 to 50 mm Hg. This error may be avoided by palpation of the radial pulse or by inflating the cuff to maximal pressure.

Ordinarily the blood pressure in the legs is not measured. Palpation of the femoral arteries largely eliminates the necessity if one is aware that the femoral pulses occasionally may be quite strong even with severe coarctation of the aorta. If this condition is suspected the pressure in the legs should be obtained using a special large cuff around the thigh and with the stethoscope placed over the popliteal artery.

Patients should be told what their blood pressure is and instructed to remember it. This may be done without unnecessary alarm by providing proper interpretation for them. With the present ease and extent of travel this information as well as knowledge of certain drug treatment is necessary for the patient to obtain proper care from a consultant or an unfamiliar physician.

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CHAPTER 26

Roentgenology of the Heart

Joseph Jorgens, M.D., Ph.D.

INTRODUCTION

IN most medical centers the roentgen examination of the heart is now accepted as a routine method in the diagnosis of heart disease. It is an extension of the physical examination. The roentgen examination of the heart is most valuable in assessing the size and shape of the heart. Abnormalities in the size and shape resulting from disease can be easily detected.

This chapter is intended to introduce a physician to this field. The material presented has been compiled from many sources. The material has proven reasonably valid in the author's experience. The bibliography was selected as representative of the extensive writings in each phase of cardioroentgenology.

This chapter deals with the anatomy of the heart, methodology and valid roentgen findings in cardiovascular disease.

THE ROENTGEN ANATOMY (SHAPE) OF THE HEART AND GREAT VESSELS IN THE POSTERO-ANTERIOR (FRONTAL) PROJECTION (FIG. 1)

The left border of the heart can be divided into four potential convexities. The superior curve represents the posterior part of the aortic arch (Fig. 1). The second curve of the left border of the heart is the pulmonary artery lying above the left bronchus. The left atrial appendage normally makes up an inconspicuous third curve. The fourth curve forms the apical heart border and represents the left ventricle.

The right border of the heart can be divided into the supracardiac segment and the cardiac segment. The supracardiac silhouette is formed by the superior vena cava in the young individual and by a superimposition of both the superior vena cava and the ascending arch of the aorta in the older individual. The cardiac border is formed by the right atrium. Occasionally the hepatic vein presents at the right cardiophrenic sulcus.

The right ventricle occupies the mid position in the cardiac silhouette and does not appear as a border structure on the frontal projection normally.

The other roentgen views are seen in Figures 2, 5 and 9.

METHODS EMPLOYED IN CARDIOROENTGENOLOGY

FLUOROSCOPY

Fluoroscopy is used primarily in the study of pulsations of the chambers of the heart and associated vessels and in the detection of calcification within the heart. The size of the heart is more satisfactorily estimated from roentgenograms.

Standard Fluoroscope[10]

The standard fluoroscope consists of an x-ray tube, table, and a fluoroscopic screen. The x-rays emitted from the tube pass into the patient and are absorbed in varying amounts by tissues of differing density. The rays not absorbed pass through the body producing an

volume Occasionally, it may be detected at the apex or by palpation of the arterial pulse A more sensitive method uses the sphygmo manometer The cuff pressure is carefully adjusted at the systolic level so that only the alternate strong beats are audible The evenly spaced beats of pulsus alternans are easily differentiated from the uneven beats of bigeminy

REFERENCES

1 Leopold, Simon S *The Principles and Methods of Physical Diagnosis* Philadelphia, Saunders, 1952
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CHAPTER 26

Roentgenology of the Heart

Joseph Jorgens M D Ph D

INTRODUCTION

In most medical centers the roentgen examination of the heart is now accepted as a routine method in the diagnosis of heart disease It is an extension of the physical examination The roentgen examination of the heart is most valuable in assessing the size and shape of the heart Abnormalities in the size and shape resulting from disease can be easily detected

This chapter is intended to introduce a physician to this field The material presented has been compiled from many sources The material has proven reasonably valid in the authors experience The bibliography was selected as representative of the extensive writings in each phase of cardioroentgenology

This chapter deals with the anatomy of the heart methodology and valid roentgen findings in cardiovascular disease

THE ROENTGEN ANATOMY (SHAPE) OF THE HEART AND GREAT VESSELS IN THE POSTERO-ANTERIOR (FRONTAL) PROJECTION (FIG 1)

The left border of the heart can be divided int[illegible]r potential convexities The superior [illegible]esents the posterior part of the aortic [illegible]1) The second curve of the left [illegible] the heart is the pulmonary artery [illegible]ve the left bronchus The left atrial [illegible]age normally makes up an inconspicu[illegible]rd curve The fourth curve forms the [illegible]l heart border and represents the left [illegible]tricle

The right border of the heart can be di[illegible]ded into the supracardiac segment and the [illegible]rdiac segment The supracardiac silhouette is formed by the superior vena cava in the young individual and by a superimposition of both the superior vena cava and the ascending arch of the aorta in the older individual The cardiac border is formed by the right atrium Occasionally the hepatic vein presents at the right cardiophrenic sulcus

The right ventricle occupies the mid position in the cardiac silhouette and does not appear as a border structure on the frontal projection normally

The other roentgen views are seen in Figures 2 5 and 9

METHODS EMPLOYED IN CARDIOROENTGENOLOGY

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Fig 3 Calcification of the aortic valve in the right anterior oblique view

Fig 4 Calcification of the anterior descending branch of the left coronary artery in the right anterior oblique view



Fig 5 Left anterior oblique view Normal male age 30 Because of a narrow anteroposterior diameter of his chest the heart extends beyond the spine Note there is no protrusion of the left ventricle as seen in Figure 6

Fig 1 A Normal heart in the posteroanterior view B A diagram of the anatomy of the heart



Fig 2 A Right anterior oblique view showing cardiac curves in an emphysematous patient B A diagram of the cardiac anatomy

larging right ventricle right atrial appendage (Fig 12) or ascending aorta

CONVENTIONAL ROENTGENOGRAPHY

An x ray unit capable of a 300 to 500 milliampere tube current is desirable because with it a short exposure time of $^1/_{15}$ to $^1/_{60}$ second is possible This short exposure time makes possible the recording of rapidly moving calcifications within the heart which are blurred out by longer exposures However for routine office roentgenograms of the heart 100 to 200 milliampere units are adequate

Positions Used for the Roentgenographic Examinations of the Heart (Fig 13)

Four views of the heart are popular since they have proved important in the evaluation of a cardiac status These are the posteroanterior 65° left anterior oblique 45° right anterior oblique and the right lateral views Barium is given routinely with the posteroanterior right anterior oblique and right lateral views

ORTHODIASCOPY[31]

Orthodiascopy is an inexpensive fluoroscopic method of accurately determining the size and shape of the heart However special equipment and considerable training are necessary In most centers the size and shape of the heart is now estimated by roentgenography

ROENTGENKYMOGRAPHY[7]

Roentgenkymography and electrokymography are the two roentgen methods of permanently recording the pulsations of the heart

By means of the roentgenkymograph the action of the heart and great vessels can be recorded graphically on an x ray film Gross increase in cardiac pulsations as is seen in aortic insufficiency may be of diagnostic value However small change in the roentgenkymographic pulsations from the usual picture may be the result of the superimposed pendular movement of the heart and does not necessarily represent pathology in the cardiac muscle or vessels[1]

Since the cost and the technical difficulties involved in producing an adequate kymogram are considerable and the additional diagnostic information obtained is small the method has not gained popular acceptance

ELECTROKYMOGRAPHY

Electrokymography is another method of recording cardiac pulsations[3, 75, 48, 38] It is still an experimental instrument with no proved clinical value[42, 20]

ANGIOCARDIOGRAPHY[13, 8, 9]

In congenital heart disease the diagnosis can be made by visualizing angiocardiographically the sequence of circulation of the blood through the heart and the size and shape of the lumen of the large vessels and of the chambers of the heart

In this method the radiopaque contrast agent is injected rapidly into a peripheral vein Biplane serial radiographs are obtained as the contrast agent passes through the heart Angiocardiography is an effective method of recognizing radiographically the presence of a shunt from the right side to the left side of the heart such as exists in some septal defects[3] In addition it is effective for recognizing a left to right shunt such as a patent ductus if the contrast agent is suddenly diluted with blood in a specific chamber or if there is a re circulation of the contrast agent through the right side of the heart[53]

Since deaths have resulted from this procedure only patients whose clinical condition demands diagnosis should have angiocardiography

Selective Angiocardiography[10]

In the diagnosis of congenital heart disease selective angiocardiography is usually performed as a compliment to catheterization In this type of angiocardiography a catheter is inserted into the antecubital vein and threaded into the heart The radiopaque agent is injected rapidly through the catheter into a selected chamber of the heart The injection at a selected site has advantages over peripheral angiocardiography[74] There is an increased clarity of the pathology because the concentrated contrast agent is injected exactly at the site where the lesion has been suggested by the clinical and heart catheteriza

image of the absorbing tissue on the fluorescent screen Dark adaptation time of at least twenty minutes is optimum for perceiving this dim fluorescent image [16] Even after adaptation a detailed image cannot be seen for only the retinal rods not the cones are activated by the dim light

Image Amplifier[9 10]

With the new fluoroscopic image amplifie an image at least two hundred times as bright as the standard fluoroscopic image is produced Prolonged dark adaptation is unnecessary The details of the image can now be perceived because the cones of the retina are stimulated by this much brighter image A camera attachment on the amplifier is available for recording heart movements [44]

Essential Steps in Cardiac Fluoroscopy [6]

Posteroanterior View

Examine rapidly the entire chest for any obvious pulmonary abnormalities Then examine the hilar structures main pulmonary arteries and aorta for pulsation and presence of calcification within these structures The amplitude of pulsation of the aorta and pulmonary artery should be compared An unusual amplitude indicates an increased stroke volume of the corresponding ventricular chamber an increased peripheral resistance or an unusual distensibility of the vessel wall Note the pulsations of the chambers of the heart and particularly the pulsation of the left ventricle If the superior part of the apex is moving outwards during the systolic movement of the diaphragmatic portion of the left ventricle an infarction of the heart should be considered [77]

If the amplitude of pulsation of a single chamber is increased an insufficiency of the associated outflow valve should be considered A decreased pulsation is usually associated with an enlarged cardiac silhouette and is either on the basis of a myocardial disease or a pericardial effusion

Right Anterior Oblique View (Patient's right anterior chest against the fluoroscopic screen, Fig 2)

In this view check to see if there is a prominent outflow tract of the right ventricle (Fig 41) check to see if there are any calcifications of the mitral or aortic valve (Fig 3),[54] or any calcification in the coronary arteries (Fig 4) [61] Calcifications in the mitral area are best seen in an 80° right anterior oblique view

Left Anterior Oblique View (Patient's left anterior chest against the fluoroscopic screen Figs 5 and 6)

In this view check for pericardial calcification along the diaphragmatic surface of the ventricles and for valve and coronary artery calcification (Figs 7 and 8) Also note the amount of projection of the left ventricle and left atrium posteriorly The *protrusion of the* left ventricle beyond the spine in the left anterior oblique view has been widely used as a *criterion of left ventricular enlargement* This criterion is not valid in individuals with deep or narrow anteroposterior chest diameters In some patients the pulsations of the right auricular appendage can be distinctly observed at the junction of the ascending aorta and the cardiac silhouette Pulsations in this area will be the auricular rhythm This rhythm can be compared to the aortic and the ventricular rhythm by observing simultaneously these structures It is possible to distinguish different degrees of heart block by this method

Right Lateral View (Patient's right side against fluoroscopic screen, Fig 9)

In this view the patient swallows barium and any displacement of the esophagus is noted If the esophagus is displaced posteriorly in the left atrial area the left atrium is enlarged (Fig 10) [46] Turn the patient into the right anterior oblique and the posteroanterior view while he is swallowing barium The esophagus is to the patient's right when it is being displaced by an enlarged left atrium If the esophagus is to the patient's left it is usually not due to an enlarged left atrium but rather due to a tortuous aorta which is pulling the esophagus with it into the left paravertebral region

Calcifications in aortic valve are often seen best in this lateral view (Fig 11) The retrosternal area is usually radiolucent This radiolucency may be encroached upon by an en

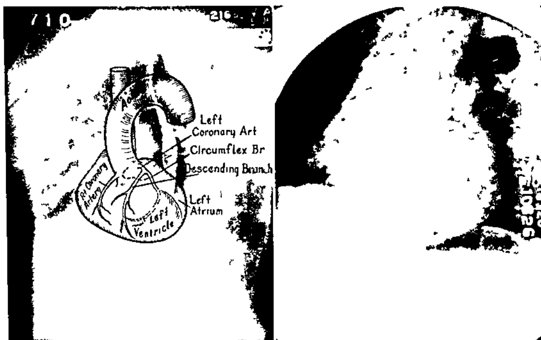


Fig 8 A A diagram of the anatomy of the coronary arteries in left anterior oblique view B Calcification in a branch of the left coronary artery

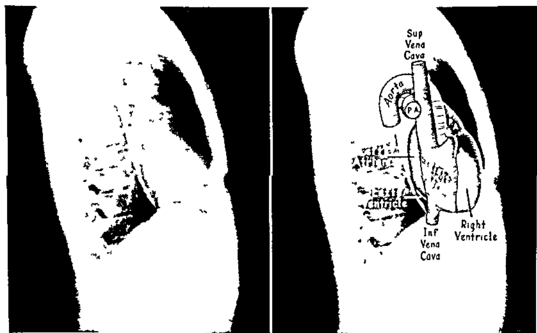
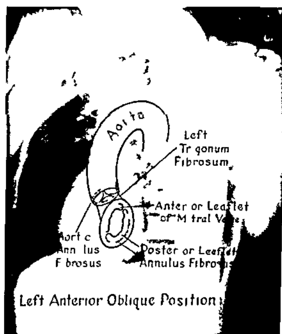


Fig 9 A Right lateral view of a normal heart B Cardiac anatomy in a normal heart

Fig 6 A Aort c ste os s The left anterior obl que v e v sho vs left ventric ılar and left ıtrial rominence Note downward and poster or protrus on of the left ventricle B A diagram of the ard ac anatomy in the left anter or obl que v ew



F g 7 A diagram of pos tion of valves



Fig 13 Conventional cardiac views A posteroanterior view B right anterior oblique view, C left anterior oblique view D right lateral view

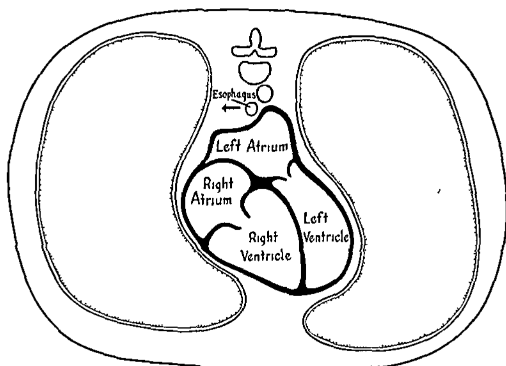


Fig 10 Cross sectional diagram of the heart showing relative position of the left atrium esophagus and aorta When the left atrium enlarges it forces the esophagus posteriorly and usually to the right



Fig 11 Aortic stenosis Calcification seen in aortic valve



Fig 12 Lateral view showing enlarged right side of the heart filling in the mid retrosternal space



Fig 13 Conventional cardiac views A posteroanterior view B right anterior oblique view C left anterior oblique view D right lateral view

tion studies A lesser amount of contrast medium is necessary when a specific site is being studied[8]

RETROGRADE AORTOGRAPHY[9,23]

Retrograde aortography is performed to establish the diagnosis of patent ductus arteriosus and of congenital aortic diseases such as coarctation and hypoplasia of the aorta This method is of special value in infants

In infants retrograde *aortography is* performed by injecting a contrast material, under pressure, into the left subclavian artery. The radiopaque material is forced against the blood stream into the aorta, picturing the aortic lumen In adults a catheter is threaded through a peripheral artery to the aorta and through this catheter the opaque medium is rapidly injected

INTERPRETATION OF ACQUIRED HEART DISEASE

In the preceding section roentgen anatomy of the heart and methodology are presented On the basis of alteration in the normal anatomy, a roentgen diagnosis is made In this section the criteria and causes for enlargement *of vessels and chambers of the heart* are discussed

LARGE AORTA (FIG. 14)

Criteria for Determining an Enlarged Aorta

The aortic arch silhouette in a PA view, from the lateral tracheal wall to the left margin of the aorta, measures less than 4 0 cm in diameter. If over 4 cm it is considered ectatic (Fig 15) When the aorta dilates, it also elongates, and the ascending aorta protrudes from the right border of the cardiac silhouette and the descending aorta, *unless buckled in* the region of the ligamentum arteriosum, lies in the left paravertebral region

Frequently views other than the frontal view delineate more clearly saccular aneurysms *of the aorta*

The diameter and length of the aorta increase with age due to progressive degeneration of the elastic tissue[19] *Increased aortic* pulse pressure hastens the degeneration of the elastic tissue causing early dilatation and elongation of the aorta

Lesions Causing Enlargement of the Aorta

In hypertensive heart disease and in aortic insufficiency (*Fig 16*) *there is commonly* a dilatation of the ascending aorta in the posteroanterior view If *the aortic insufficiency* is on the basis of syphilis rather than rheumatic heart disease, a linear calcification in the ascending aorta is a typical diagnostic finding[61] Certain congenital heart diseases, such *as patent ductus, coarctation of the aorta, and* pseudotruncus arteriosus frequently manifest enlarged aortas[28]

SMALL AORTA

The small aorta is usually associated with conditions having a low left ventricular output *A small aorta is accepted as part of the typical* roentgen picture in pure mitral stenosis and in interatrial septal defect (Fig 17)

LARGE PULMONARY ARTERY

Criteria for Determining an Enlarged Pulmonary Artery

The second convexity along the left border of the cardiac silhouette is considered the radiologic pulmonary artery (Fig 18) If a line is drawn vertically from the superior margin of the radiolucent left bronchus to the *superior margin of the left main pulmonary* artery segment, a radiologic dimension is obtained which varies with the true anatomic size of the pulmonary artery *If this dimension* measures over 3 cm in diameter, it is enlarged The dimension is a composite measure of enlargement of the main pulmonary artery segment and the elongation of the left main pulmonary artery (Fig 15)

When the main pulmonary artery segment

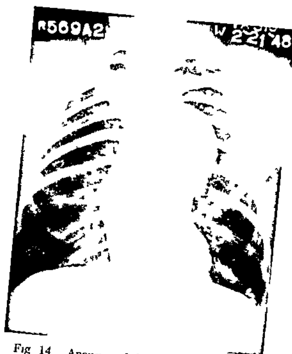


Fig 14 Aneurysmal dilatation of the aorta

Aorta
25-40 mm
Pulm. Artery
20-28 mm
Left Bronchus
Waist of Heart
55-75 mm

Fig 15 Range of normal measurements in 90 of males in a selected sample

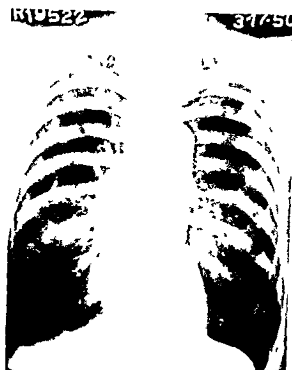


Fig 16 Dilatation of ascending aorta resulting from luetic aortitis Note calcification in ascending aorta



Fig 17 Right aortic arch No clinical findings of disease
Fig 18 Anteroposterior planigram showing positions of aorta and pulmonary artery

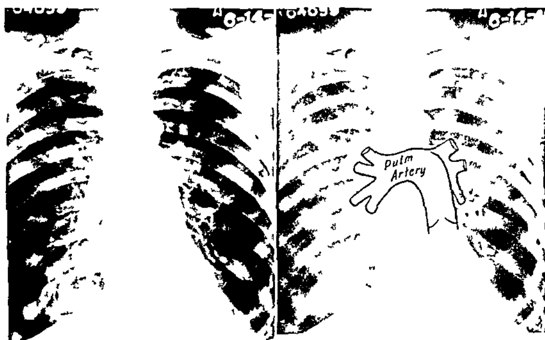


Fig 19 A Enlargement of the outflow tract of the right ventricle resulting from severe emphysema B Diagram of outflow tract anatomy

enlarges the hilar arteries usually enlarge When severe pulmonary hypertension ensues the outflow tract of the right ventricle enlarges widening the horizontal waist of the heart at at the level of the junction of the second and third curve of the left heart border (Fig 19)

The right anterior oblique view is probably the best view for easily recognizing an enlarged undivided pulmonary artery segment In this view the pulmonary artery segment becomes increasingly convexed as the pulmonary artery dilates and elongates (Fig 41)

Lesions Causing Enlargement of the Main Pulmonary Artery Segment

I Pulmonary Hypertension Resulting from Increased Resistance in the Pulmonary Vascular System

Left-sided Failure Pulmonary hypertension often develops from left sided failure resulting from lesions such as mitral or aortic disease Left sided failure can be recognized as a cause of the pulmonary hypertension by the presence of an enlarged left atrium congested pulmonary veins and edema of the pulmonary parenchyma (Fig 20)

Lung Disease Any disease of the lung which reduces the total vascular capacity of the lungs resulting in increased resistance to blood flow will cause pulmonary hypertension

Narrowing of the arterioles secondary to spasm acute inflammation intimal or medial fibrosis thrombosis or stretching of the arterioles may result in pulmonary hypertension (Fig 21)

On a roentgenogram the specific lung abnormality such as emphysema or fibrosis is often recognized as the cause of the pulmonary hypertension and enlargement of the pulmonary artery segment

II Left to Right Shunts

Pulmonary hypertension also results from left to right shunts owing to increased pulmonary blood flow Early the left to right shunts are identified by the increased pulmonary vascular pattern Later with the development of chronic severe pulmonary



Fig 20 Interatrial septal defect (ostium primum) with left ventricular failure Age 65 The left to right shunt increased markedly when the left ventricle failed

Fig 21 Primary pulmonary hypertension Note large undivided pulmonary artery segment central vessels and right atrium

Fig 22 Mitral stenosis Note third curve enlargement along the left heart border

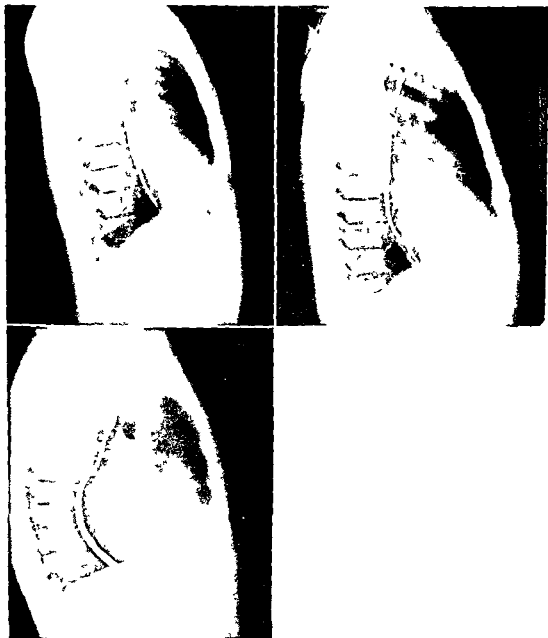


Fig 23 A Esophagram showing normal indentations of the esophagus B Slight deviation of the esophagus posteriorly resulting from left atrial enlargement C Esophagus pulled posteriorly by elongating aorta The esophagus deviated to the patient's left in the posteroanterior view





Fig 24 Severe calcification in the mitral valve Male age 57 Mitral stenosis with slight insufficiency
Fig 25 Mitral insufficiency Note enlarged left atrium and ventricle

hypertension the peripheral vascular tree is partially obliterated and becomes disproportionately small compared to the central pulmonary arteries [6]

III *Pulmonary Valve Stenosis*

Classically there is a disproportionate enlargement of the main pulmonary artery segment compared to the right hilar shadow in pulmonary valve stenosis (see chapter on congenital heart) [8]

SMALL PULMONARY ARTERY

A decreased size of the main pulmonary artery is associated with congenital heart lesions such as tetralogy of Fallot and other hypoplasis of the outflow tract of the right ventricle A loss of the second curve of the left border of the heart is seen in certain types of transpositions of the great vessels (see chapter on congenital heart) [9]

LARGE LEFT ATRIUM

The exact size of a cardiac chamber cannot be measured since all borders of a chamber cannot be defined on a roentgenogram In the cardiac silhouette each curve represents a specific chamber Any disproportionate protrusion of a cardiac curve suggests an enlargement of the chamber which the curve represents

Criteria for Determining Enlargement of the Left Atrium

When the left atrium is minimally enlarged the left border of the heart straightens As enlargement increases an obvious third curve is formed (Fig 22) If the left atrium is very large either a double density or a double curvature of the right border of the heart is apparent

The barium filled esophagus is deviated usually to the right and posteriorly when the left atrium is enlarged Either the right lateral view or right anterior oblique view demonstrates this deviation In less than 3% of cases of enlarged left atria the esophagus may be pushed to the left by the left atrium or coincidentally pulled to the left by an elongated aorta (Fig 23) [31]

The validity of the roentgen findings in cases

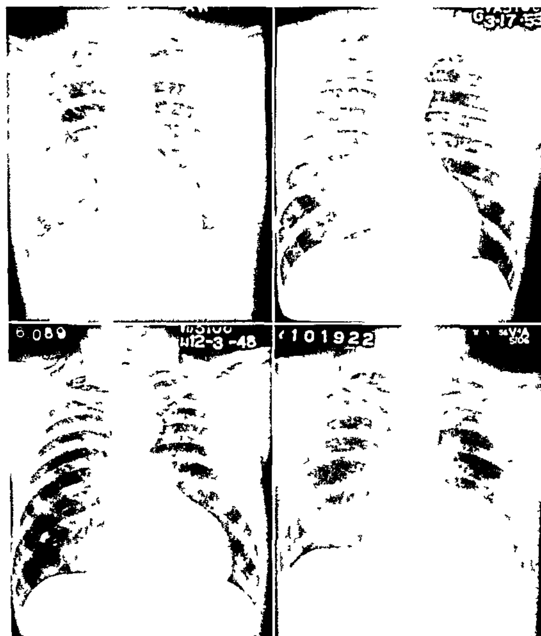


Fig 26 Degrees of enlargement of the left ventricle in different patients

of left atrial enlargement has been confirmed by clinical surgical and post mortem experience About 3% of normal medical students will have a slight posterior displacement of the barium filled esophagus in the upright lateral roentgenogram[41]

Lesions Causing Enlargement of the Left Atrium

1 Stenosis of the Mitral Valve

The amount of enlargement of the left atrium is dependent upon the pressure in the





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The validity of the roentgen findings in cases



Fig 29 Left anterior oblique shows right sided enlargement Note the normal left ventricle does not overlap the spine

Fig 30 Male age 41 Posteroanterior view shows calcification in the descending branch of left coronary artery Severe coronary symptoms



Fig 31 A Left anterior oblique view shows calcification of the circumflex branch of left coronary artery B Calcification in right coronary artery in the left anterior oblique view Coronary insufficiency was present



Fig 27 Left ventricular enlargement in A left anterior oblique view and in B right lateral view



Fig 28 Male age 40 Essential peripheral hypertension

left atrium and the state of the left atrial wall and supporting tissues Small calcifications in the mitral valve radiographically are characteristic of mitral stenosis [54] Typically the left ventricle is normal in size (Fig 22)

The findings of a calcified mitral annulus fibrosus does not necessarily indicate a significant mitral lesion However, there may be an associated thickening of the mitral valves causing some degree of mitral stenosis The etiology of rheumatic fever should be strongly suspected when a calcified mitral annulus

Fig 33 Coronary occlusion associated with pneumonia and pleural effusion
Fig 34 Thickened pleura over the apex of the heart resulting from previous transmural myocardial infarction

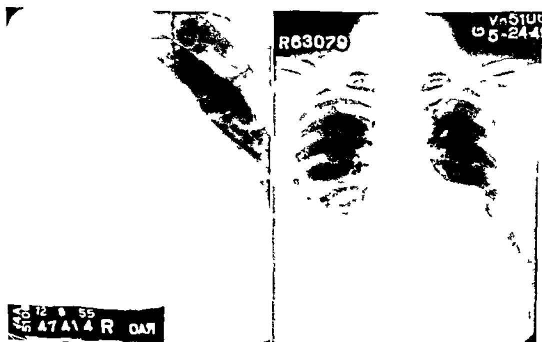


Fig 35 Calcification of the myocardium and pericardium resulting from a previous myocardial infarction Apical distribution is characteristic
Fig 36 Aneurysm of the left ventricle Note square appearance of left ventricle

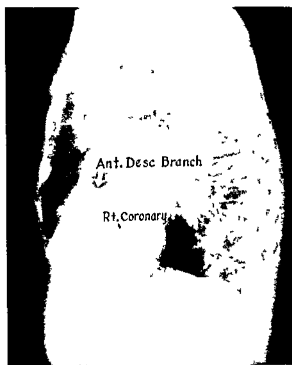


Fig 32 Coronary calcifications in the lateral view

fibrosus is found in a patient under 50 years of age (Fig 24)

In patients with chronic congestion or with bouts of recurrent congestion one occasionally sees small round opaque densities (hemosiderosis), linear densities at the costophrenic sulci,[34 51] emphysema and enlarged pulmonary arteries

II. Insufficiency of the Mitral Valve

Classically, an enlarged left atrium, with an increased amplitude of pulsation, and an enlarged left ventricle, characterize insufficiency of the mitral valve (Fig 25) This increase in amplitude of left atrial pulsation is caused by regurgitation of blood through the incompetent mitral valve early in left ventricular systole Usually this increased amplitude cannot be distinguished from the range of amplitude of the normal left atrium

Calcification of the mitral annulus may occur in the older age group causing enough rigidity of the annulus to result in mitral insufficiency [52]

Insufficiency, resulting from rupture of the papillary muscle of the left ventricle caused by a myocardial infarction, is difficult to recognize radiologically

III. Arrhythmias

A slightly enlarged left atrium is seen in atrial fibrillation without any clinical evidence of mitral disease

IV. Atrial Infarction[58]

Idiopathic dilatation of the left atrium may be associated with an insufficiency of the branches of the coronary arteries supplying the left atrial wall Usually, however, other branches of the coronary arteries are also involved leading to a generalized dilatation of the heart

LARGE LEFT VENTRICLE

Criteria for Determining the Presence of an Enlarged Left Ventricle

When the left ventricle is enlarged, the apex of the heart extends beyond the midclavicular line (Fig 26) The inferosuperior diameter of the left ventricular curve increases in size

The enlarged left ventricle protrudes towards the spine near the diaphragm in both the right lateral and the left anterior oblique views (Fig 27)

To distinguish hypertrophy of the left ventricle from dilatation is usually impossible Concentric hypertrophy of the left ventricle, with ectasia of the aorta resulting from essential peripheral hypertension, causes the heart to assume early a transverse lie within the chest (Fig 28)

Right ventricular enlargement may be confused with left ventricular enlargement In the absence of thoracic deformity, left ventricular enlargement is definitely present if the second and third curves of the heart are normal in size and the apex of the heart extends beyond the midclavicular line If the second and third curves are also enlarged right ventricular enlargement may be present (Fig 29)

Lesions Causing Enlargement of the Left Ventricle

I Hypertensive Cardiovascular Disease Resulting from Increased Peripheral Resistance and/or Blood Flow

In middle aged patients hypertension may be present without enlargement of the left

Fig 41 A Right anterior oblique view showing enlargement of undivided segment of the pulmonary artery B A diagram of the anatomy of the right ventricular outflow tract

g 42 Right anterior oblique Mitral lesion Esophagus is pushed posteriorly and to the right by ilarging left atrium Increased prominence of right ventricular outflow tract resulting from pul ry hypertension

43 Heart dimensions The summation of the median right and left dimensions divided by ansverse diameter of the chest gives the cardio-thoracic ratio This ratio is less than 55 in nor M R is the median right measurement

Fig 37 Aortic stenosis Note slight left ventricular enlargement
Fig 38 Lateral view Aortic stenosis and luetic aortitis Note calcification in aortic valve (lower arrow) Upper arrow shows calcification in ascending aorta owing to luetic aortitis

Fig 39 Aortic regurgita ... ascend ... aorta
Fig 40 Luetic aortitis ... mini

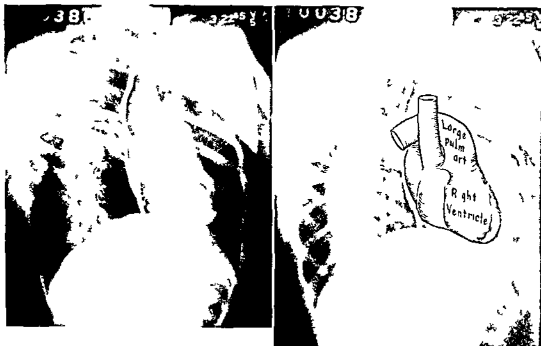


Fig 41 A Right anterior oblique view showing enlargement of undivided segment of the pulmonary artery B A diagram of the anatomy of the right ventricular outflow tract

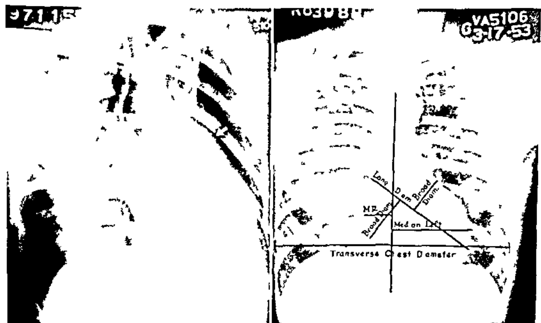


Fig 42 Right anterior oblique Mitral lesion Esophagus pushed posteriorly and to the right by an enlarging left atrium Increased prominence of right ventricular outflow tract resulting from pulmonary hypertension

Fig 43 Heart dimensions The summation of the median right and left dimensions divided by the transverse diameter of the chest gives the cardio-thoracic ratio This ratio is less than 55 in normals M R is the median right measurement



Fig 44 A Funnel chest in posteroanterior view Note heart displaced into left chest B Funnel chest in lateral view (different patient)

ventricle[47] Gradually however depending on the coronary sufficiency and on the degree and duration of the hypertension left ventricular prominence occurs

Essential hypertension produces a more characteristic picture The heart assumes a transverse lie in the chest and the ascending aorta becomes prominent The point of junction of the ascending aorta with the right atrium is abnormally close to the diaphragm (Fig 28)

II Coronary Heart Disease[9]

A normal sized left ventricle is commonly found in patients having an acute infarction of the myocardium without previous history of heart disease In contrast a large left ventricle is found in patients who have had repeated myocardial infarctions or long standing insufficiency of the coronary artery associated with systemic hypertension

A diagnosis of potential arteriosclerotic heart disease can be suggested if calcifications are found within the coronary arteries (Figs 30 31 and 32)[17 18] Calcific deposits in the intima and media of the coronary arteries can be easily recognized with the image amplifier type of fluoroscope[6] Although the presence of these calcifications firmly establish the diagnosis of arteriosclerosis of these vessels clinical symptoms may not be present[45]

When a small subendocardial infarction occurs usually no enlargement of the left ventricle occurs and the diagnosis cannot be made by roentgenography On the other hand a transmural myocardial infarction causing inflammation of the pericardium and of the pleura over the apex of the heart produces a typical radiographic picture characterized by an enlarging silhouette a left pleural effusion and a left lower lobe pneumonia (Fig 33) When the acute stage subsides these abnormal findings may completely resolve[14] Often a previous myocardial infarction can be recognized by the stigmata of a slightly enlarged left ventricle adhesions between the apex of the heart and the chest wall and obliteration of the left costophrenic sulcus by thickened pleura (Fig 34) Calcification of the infarcted myocardium and over



Fig 47 Pericardial effusion Note subepicardial fat line is more than three millimeters within the cardiac border

Fig 48 *Pericardial effusion Markedly enlarged cardiac silhouette with loss of usual curvatures*

The fibrocalcifying process of aortic stenosis may be superimposed upon a long standing aortic insufficiency[4] The typical findings of aortic insufficiency are then lost when this association occurs

SMALL LEFT VENTRICLE

In acquired heart disease a small left ventricle is associated with a small sized heart It is seen in such diseases as Addison s disease chronic asthma emphysema severe mitral stenosis and chronic illnesses

LARGE RIGHT VENTRICLE

Criteria for Determining the Enlargement of the Right Ventricle

No good roentgen finding of early right ventricular hypertrophy is known in the frontal view

The lack *of a valid* roentgen finding for right ventricular hypertrophy on the frontal projection is not crucial because enlarged pulmonary arteries are presumptive evidence of a hypertrophied right ventricle

When the right ventricle dilates there is usually an increase in the median right measurement and in the width of the waist of the heart in the frontal projection (Fig 15) This widened waist is a horizontal measurement from the right side of the cardiac silhouette to the left side at the level of the lower border of the left main bronchus This measurement may be widened by an enlarged ascending aorta right atrium left atrial appendage or undivided pulmonary artery segment The significance of this measurement varies with the specific chamber or vessel which is enlarged

The most valid roentgen finding of right ventricular enlargement is the convexity of the outflow tract of the right ventricle in the right anterior oblique view (Fig 41)

In the right lateral view a decrease in the radiolucency of the retrosternal space may result from an enlarged right ventricle However an enlarged right atrial appendage *or*

dilated aortic arch may also fill in this radiolucent area

A characteristic picture of right ventricular enlargement is occasionally seen in pulmonary valve stenosis in the left anterior oblique view. The right side of the heart which is anteriorly located is bulbous while the left side of the heart tapers almost to a point posteriorly and is situated some distance above the diaphragm (*see chapter on congenital heart*)

Lesion Causing Right Ventricular Enlargement

I Pulmonary Hypertension Owing to Increased Peripheral Resistance and/or Blood Flow

Early in pulmonary hypertension only the central pulmonary arteries increase in size. Later with increasing pulmonary pressure the right ventricle dilates. If left sided failure is the cause of the pulmonary hypertension the left atrium is also enlarged. *In contrast if the pulmonary hypertensive state is the result of primary parenchymal or vascular disease of the lung* the left atrium is normal in size (*Fig 42*)

II Congenital Heart Disease (See chapter on congenital heart)[18]

Right ventricular enlargement results from a shunt in the heart or in the pulmonary vessels. This enlargement occurs especially if pulmonary hypertension ensues

An enlargement of the right ventricle also results from a congenital stenosis of the pulmonary valve

LARGE RIGHT ATRIUM

Criteria for Determining the Presence of Right Atrial Enlargement

When the right atrium is enlarged the median right dimension of the heart is increased. In addition the diameter extending from the junction of the right atrium and superior vena cava to the right diaphragm is increased in size

In general the right atrium will enlarge in lesions resulting in right ventricular failure and in lesions of the tricuspid valve. If there is an increase in the blood volume this chamber will increase in size

GENERALIZED ENLARGEMENT OF THE CARDIAC SILHOUETTE PRESENT STATUS OF HEART MEASUREMENT[13, 48]

The significant place of roentgenology in heart disease today has been the result of emphasis on detecting specific chamber and vessel enlargement rather than on stressing the exact measurement of the over all size of the heart. A specific chamber may be moderately enlarged due to advanced heart disease yet the overall size of the heart is within normal limits

Ungerleider's nomogram for heart size is probably the most popular method for determining over all heart enlargement[60]. It is based upon a prediction formula for the transverse diameter of the heart using height and weight as predicting variables

When the height and weight of the patient are not available the cardio thoracic ratio is used (Fig 43)[33]

Cardio-thoracic ratio = $\frac{\text{Transverse diameter of the heart}}{\text{Transverse diameter of the chest}}$

Any cardio thoracic ratio over 55 indicates cardiac silhouette enlargement[8]. Neither the cardio thoracic ratio nor the transverse diameter of the heart is a valid measure of heart size in mitral disease in extremes of body build or in chest deformities (Fig 44). *In order to recognize the presence of these conditions* cardiac fluoroscopy and appropriate radiograms in different views should be obtained

Area and volumetric estimations of the heart size have been used in several centers. They have not proved clinically popular because of the increased time and equipment necessary for computation with questionable improvement in results[20 27 43]

Lesions Causing Generalized Enlargement of the Heart

I Ventricular Failure

A generalized enlargement of the heart

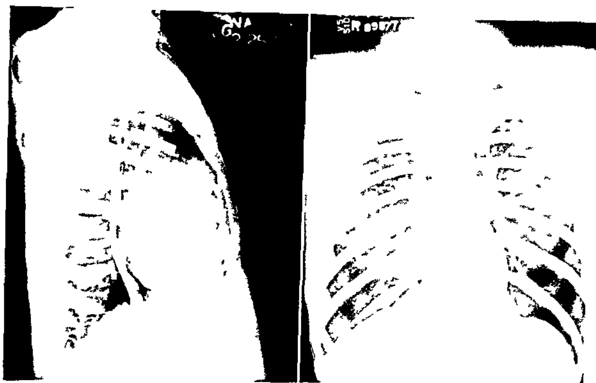


Fig 49 Right lateral view Calcification within the pericardium resulting from old tuberculous pericarditis

Fig 50 Posteroanterior view showing heart disproportionately small compared to chest cage This disproportion is often seen in emphysematous patients This patient had multiple psychosomatic complaints with no evidence of emphysema

results from right and left ventricular failure A variety of conditions such as coronary insufficiency myocarditis hypertension valvular disease and obscure metabolic conditions of the myocardium can result in a generalized enlargement of the heart (Fig 45) Usually the left ventricle fails first followed by failure and enlargement of the right ventricle (Fig 46) Congestion of the lungs may be minimal when both ventricles have failed

In failure due to arteriosclerotic heart disease or myocarditis pulsations of both ventricles are diminished but in high output failure such as in hyperthyroidism or peripheral arteriovenous fistula the ventricular pulsation is increased in amplitude

II *Increased Blood Volume*

The heart acts as a storehouse for blood[36] When the blood volume of the body increases the heart enlarges This increased blood volume results from bodily retention of salt and fluid such as is present in steroid therapy pregnancy Cushing's disease renal failure and certain types of liver failure

III *Increased Stroke Volume*

In marked bradycardia with a normal cardiac output generalized enlargement of the heart is commonly seen

IV *Pericardial Effusion*

The generalized enlargement of the cardiac silhouette caused by pericardial effusion can be readily recognized if the subepicardial fat line can be detected within the apical shadow of the heart If pericardial effusion or thickened pericardium is present this radiolucent line lies more than 3 mm within the superior apical cardiac border (Fig 47)[30] In pericardial effusion the border pulsations are diminished If the pericardial effusion is massive the usual curves of the left border of the heart disappear (Fig 48) A calcified

pericardium often results from a tuberculous pericarditis (Fig 49)

GENERALIZED DECREASE IN SIZE OF CARDIAC SILHOUETTE

A small heart is seen in severe asthma emphysema decreased blood volume such as seen in Addison's disease certain psychosomatic states and in chronic debilitated states (Fig 50)

OUTLINE FOR THE INTERPRETATION OF CONGENITAL HEART DISEASE [6, 13, 25, 28, 43, 58]

The roentgenology of congenital heart disease has become a subspecialty of radiology The roentgen methods employed in the diagnosis of congenital heart disease are three plain films angiocardiograms and heart catheterization

BASIC STEPS IN THE ROENTGEN DIAGNOSIS OF CONGENITAL HEART DISEASE BY ROUTINE ROENTGENOGRAPHY

(1) Determine if the heart is normal in size shape and position

(2) Determine if the pulmonary vasculature is normal decreased or increased in size

(3) Differentiate between congenital and acquired heart disease if possible

Usually the clinical findings help considerably in differentiating a mitral lesion or rheumatic myocarditis from congenital heart disease

The Correct Assessment of the Pulmonary Vasculature

The correct diagnosis of a congenital lesion is dependent largely upon the decision as to whether the pulmonary vasculature is increased decreased or in any way abnormal Since there is no acceptable way to measure quantitatively the amount of pulmonary vascularity this decision is based upon the subjective opinion of the observer

If the vascularity of the lungs is increased on the routine roentgenograms and the patient is not cyanotic one of four lesions is usually present a patent ductus arteriosus an interventricular septal defect an interatrial or connection into the right atrium As the patient matures the patient with the patent ductus arteriosus tends to have a larger aorta than the patient with a septal defect Otherwise the diagnosis will depend largely on the findings at heart catheterization An anomalous pulmonary venous drainage into the right atrium is occasionally recognized by the doughnut shaped mass seen in the superior mediastinum The mass represents enlarged veins

If there is increased vascularity in a non cyanotic child the final diagnosis is usually obtained through heart catheterization

A decreased vascularity of the lung fields indicates that blood is being shunted away from the lungs This is caused by an obstruction in the pulmonary artery outflow tract of the right ventricle or at the tricuspid valve Many eponyms are applied to these lesions depending on the position of the obstruction and the site of the shunt

A final diagnosis of a cyanotic heart defect is obtained through angiocardiography

A table of the classical roentgen findings in congenital heart disease is provided below

KEY FINDINGS IN CONGENITAL HEART DISEASE

Increased Vascularity

Patent Ductus Arteriosus

(1) Normal to large aorta

(2) Normal to large left ventricle and left atrium

(3) Normal to large pulmonary artery and left ventricle

Interventricular Septal Defect and Reversing Interventricular Defect (Eisenmenger's syndrome)

(1) Small size aorta
(2) Normal to large left atrium
(3) Normal to large right ventricle and pulmonary artery

Interatrial Septal Defect (ostium secundum)

(1) Small sized aorta
(2) Normal sized left atrium unless associated with mitral valve deformity
(3) Normal to large right ventricle and pulmonary artery

Anomalous Pulmonary Venous Drainage into Left Vertical Vein

(1) Superior mediastinal mass
(2) Enlarged right ventricle and pulmonary artery

Atrioventricular Canal (ostium primum defects)

(1) Normal sized aorta
(2) Enlarged left atrium
(3) Enlarged right ventricle and pulmonary artery

Transposition of the Great Vessels (cyanotic patient)

(1) Narrow superior mediastinum (great vessels)
(2) Generalized enlargement of the heart
(3) No thymic shadow

Decreased Vascularity

Pulmonary Stenosis with Interventricular Defect (Tetralogy of Fallot)

(1) Concave pulmonary artery segment
(2) Normal to large aorta
(3) *Normal to large right ventricle*
(4) Normal sized heart

Ebstein's Disease

(1) General enlargement of the heart
(2) Decreased pulmonary vascularity

Tricuspid Atresia with Interatrial Septal Defect

(1) Large left atrium and ventricle
(2) Flat right side of the heart

True Truncus with Pulmonary Flow from Bronchial Arteries

(1) Enlarged aortic like shadow
(2) Normal sized heart
(3) Concave pulmonary artery segment

Miscellaneous Lesions

Coarctation of the Aorta

(1) Enlarged left ventricle and atrium
(2) Rib notching
(3) Dilated left subclavian
(4) Medial indentation of descending aorta

Pulmonary Valve Stenosis

(1) Disproportionate enlargement of undivided pulmonary artery segment compared to right hilar shadow
(2) Normal vascular markings
(3) Right ventricular enlargement

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CHAPTER 27

Principles of Electrocardiography

C. Aravanis, M.D., and A. A. Luisada, M.D., F.A.C.P., F.A.C.C.P.

INTRODUCTION

The science which deals with the study of the electrical phenomena produced by the heart during the cardiac cycle is called electrocardiography. The graphic record of the electrical potentials of the heart is called electrocardiogram and the instrument with which this record is obtained is the electrocardiograph.

A good grasp of electrocardiography can be obtained only through a thorough understanding of the physical basis of the process involved. Unfortunately the electrical theories and the mathematics necessary for this understanding are somewhat difficult. For this reason many try to explain empirically the tracings. The resulting mistakes are known to any consulting cardiologist.

The ECG is a necessary part of the clinical examination of any cardiac case. A complete interpretation of the ECG requires collateral information. The history, a tentative diagnosis, the use of drugs and the level of blood pressure help in formulating a correct report. A comparison with previous electrocardiograms is often essential.

It should be kept in mind that the ECG does not supply information about the mechanical events of the heart muscle and the cardiac valves and about the cardiac output. It is unwise in most cases to base prognosis or treatment on the ECG only.

APPARATUS

STRING GALVANOMETER

It has been known for a long time that the muscle tissue produces and transmits electric currents. Koelliker and Mueller in 1856 demonstrated action currents associated with the heart beat. Waller and Ludwig in 1887 were the first to register the currents of the contracting heart with a capillary electrometer. However it was only in 1903 that W. Einthoven developed a new recording instrument, *the string galvanometer*, which could be used for accurate registration of the currents of the human heart. This instrument consists of a fine metal coated quartz string suspended in the field of a powerful magnet. The current flowing in this string deflects it in a direction perpendicular to the magnetic lines of force which run from the north to the south pole of the magnet. It is the relation of these two fields to each other that causes movements of the string (Fig. 1). Practical rules for predicting the movements of the string in any instance have been developed by Ampere and by Fleming. The image of the string is magnified by a microscope and projects onto a moving strip of photosensitive paper. The standard sensitivity is 1 cm per 1 mv. In order to record an electrocardiogram one end of the string is connected with the right arm of the patient, the other with the left arm. This connection is called lead I. In the same way other leads may be recorded. A central box contains a rheostat and a battery. The current of the latter is used in order to balance

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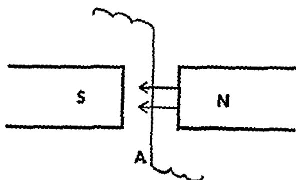


Fig. 1 String galvanometer S and N represent the two poles of the magnet The arrows represent the magnetic field and A represents the string

currents of injury, cutaneous currents, or extraneous currents, and for standardization of the sensitivity of the string

OSCILLOGRAPH

It consists of a narrow loop of wire placed in a permanent magnetic field The upper part of the loop is supported by a small pulley, while the free ends are connected to binding posts Whenever a current flows through the wire, a force arises which tends to twist the loop from the resting position A small mirror which rotates with the loop reflects a beam of light which records the movements The deflections will be proportional to the current passing through the loop

AMPLIFIER TYPE ELECTROCARDIOGRAPHS

High sensitivity oscillographs were used in the past Sturdy and less sensitive oscillographs are used in modern, portable apparatus Vacuum tube amplifiers are used to magnify the relatively small currents of the heart so that they may be recorded by these apparatus

DIRECT WRITING ELECTROCARDIOGRAPH

There are several types, all operating on the oscillograph principle The output voltage is large enough so that a writing arm traces the record on special paper In certain models, the tip of the stylus is heated while others have a special ink-writing device

ELECTRODES

Electrodes are made from German silver The currently used *limb electrodes* are 3 × 5 cm in size for adults and 2 × 2 cm for infants They are held in place by means of rubber straps The *precordial electrodes* must be small in order to pick up the currents of certain parts of the heart A round electrode of 3 cm in diameter is currently used in adults while, in children, an electrode of 1 5 cm in diameter should be preferred For the *esophageal* leads, a standard duodenal catheter is used, it ends in a metal olive which is connected to the cable by a wire passing within the catheter The *intracardiac electrode* is introduced into the heart by means of a Cournand catheter Thin walled, flexible electrodes are used for *direct leads* from the surface of the heart, and very thin electrodes are employed for intramural potentials *Needle electrodes* are used in animals

STANDARDIZATION

The electrocardiograph is standardized in such a way that a current of 1 millivolt gives a deflection of 1 cm on the film A signal wave of 1 mv for a fraction of a second must be recorded in each lead The rectangular deflection which results, enables the observer to ascertain the characteristics of the apparatus (sensitivity, fidelity, accuracy) If the ECG waves overshoot the paper, as occasionally in the precordial leads, it is necessary to cut down the sensitivity to $^1/_2$ the normal such tracing should be marked N/2 On the other hand, if the patient's tracing has only small deflections, the sensitivity should be increased and the tracing should be marked as 2N or 3N

ARTIFACTS

Several artifacts may mar an electrocardiographic tracing

(1) *Alternating Current Interference* The

record is characterized by small regular oscillations at 60 cycles per second. This is due to an alternating current field which exists in the vicinity of the patient and is greatly favored by poor contact of the electrodes or interruption of the circuit.

(2) *Muscular Tremor.* It is characterized by fine irregular oscillations of the baseline. Tense patients, unnatural and rigid position of the extremities, cold environment, Parkinsonism or hyperthyroidism are usually responsible.

(3) *Wandering Baseline.* This is usually the result of loose or dirty electrodes. Regular undulations due to respiration may be occasionally observed in the chest leads. They seem to be due to displacement of the heart in regard to the electrodes.

(4) Improper characteristics of the apparatus may be revealed by either *overshooting* or *damping* of the square wave of calibration. If either of them is present, the apparatus should be sent for repair.

(5) A high resistance of the skin, the apical thrust (chest leads), sudden movements of the patient, or shaking of the apparatus (any lead) may also cause artifacts.

MOUNTING

Many methods of mounting the ECG exist. The best is to mount the tracings in folders or cards having the same size as the case histories. Slotted paper folders are practical but add to the thickness of a folder.

ELECTROPHYSIOLOGY

Every cellular activity produces electric forces, and this is particularly true in the case of muscles. In order to better understand the electrical phenomena of the heart, *a muscular strip* can be taken as an example. It can be considered as part of the free wall of the left ventricle extending from the endocardium to epicardium and, in order to further simplify the problem, this strip can be considered as a single cell.

BERNSTEIN'S MEMBRANE HYPOTHESIS

Our fundamental concepts of the electrical phenomena of living tissues are still based on this hypothesis which was advanced in 1913. According to it, each element of a resting muscle is surrounded by a semipermeable membrane which is permeable to the positive ions (cations) and impermeable to the negative (anions). While the cations pass through freely, the anions are held back, so that a condition of equilibrium is established between positive charges at the outer surface of the membrane and negative charges at the inner surface. In this stage *K ions inside the cell* are about 50 times more numerous than those outside. A membrane which is the seat of such a double layer of ions has been referred to by physiologists as *polarized* (Bayliss, 1918).

RESTING OR POLARIZED CELL

When a living cell is in a resting state, a difference of potential exists across its membrane. On the outer surface there are positive charges and an equal number of negative charges exists at the inner surface (Fig. 2).

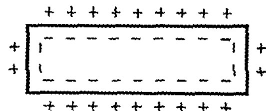


Fig. 2. Polarized cell or muscle strip. Positive charges are on the outer surface, negative charges on the inner.

Each positive-negative pair is called *dipole*. Because of the high electric resistance of the membrane, no current flows across it in this stage. It has been proven by the use of microelectrodes that a difference in potential of 65 to 95 mv. is present in nerve and muscle fibers

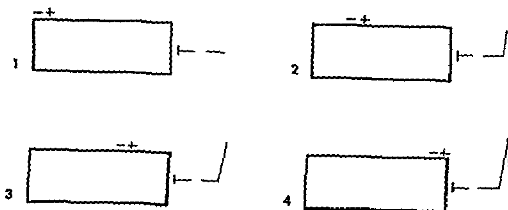


Fig 3 Process of depolarization (1) Polarized cell (2) Depolarization has started *in a left to right direction with the positive charges in front and the negative behind* (3) The process of activation has continued (4) Completely depolarized cell A *positive* deflection is recorded

This difference is called the "membrane resting *potential*"

DEPOLARIZATION OR ACTIVATION

When a resting cell is stimulated by electrical, chemical, or mechanical means, the following changes take place The resistance of the membrane decreases to about 1/50, as evidenced by an abrupt diminution of its impedance, and it becomes permeable to both anions and cations, permitting a free flow of ions in both directions As positive charges pass across the membrane, each point becomes negative in reference to the next The net effect of this immigration of ions is that the inside of the cell contains in this stage a predominant number of Na ions and becomes positive in reference to the outside which contains a greater number of K ions The front of depolarization starts from the point or area of stimulation and moves perpendicularly to the longitudinal axis of the cell, it is *preceded by positive ions and followed by negative ions* If a record of this process is made by means of a galvanometer, a wave known as the *wave of depolarization* is recorded (Fig 3)

REPOLARIZATION OR RECOVERY

Following depolarization, a restitution of the physicochemical processes promptly begins, and the positive and negative charges return to their original respective positions across the membrane This new process is called *repolarization* and, in experimental conditions, starts at the same point where depolarization had started *The front of repolarization is preceded by negative ions and followed by positive ions* The positive charges move back toward the external surface while the negative charges return inside the membrane, which becomes progressively polarized again The boundary between depolarized and repolarized muscle moves continually until the whole process is completed (Fig 4) In the normal, intact human heart, repolarization normally proceeds in a direction which is *opposite* to that of depolarization (from epicardium to endocardium) Repolarization is a slower process than depolarization, and the difference of potential is smaller As lesser magnitude and greater duration of the process of repolarization are proportional, the area included in the area of the wave of repolarization is the same as that included in the area of the wave of depolarization Both processes of depolarization and repolarization constitute the *electrical systole*

INTRINSIC DEFLECTION

It represents the arrival of the dipole of activation beneath the exploring electrode (see below) and signifies that that small area of muscle is activated It corresponds to a line which descends suddenly from the point

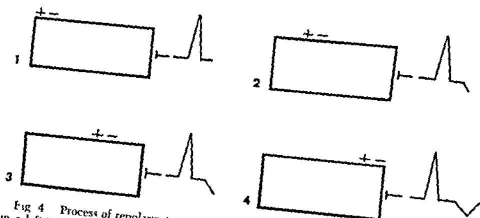


Fig 4 Process of repolarization (1) D...
in a left to right ...
The process ...
deflection is r... ...arted
(3)
... A negative

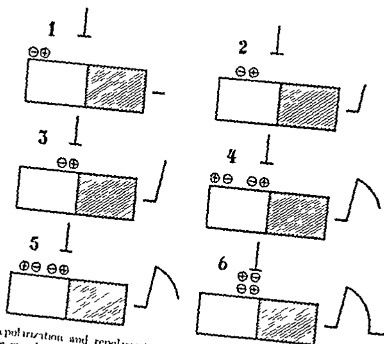


Fig 5 Depolarization and repolarization of an injured cell (1) The injured part (shaded) is less positive in relationship to the uninjured part Current is flowing from the uninjured to the injured part during diastole but the produced deflection is neutralized by the compensating current (2) Depolarization of the uninjured part has started in a direction from left to right (3) Depolarization is arrested by the boundary and an upward deflection is recorded (4) Repolarization of the uninjured part has started from left to right and the relative positivity of the injured part gradually decreases (5) The process of repolarization has continued (6) Repolarization is completed in the uninjured part A curve with an upward RS-T displacement is recorded (From Sodi Pallares New Bases of Electrocardiography St Louis, Mosby 1956)

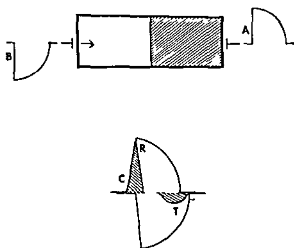


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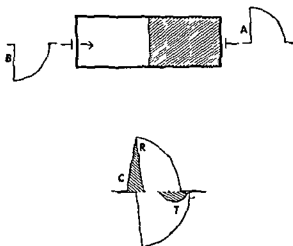


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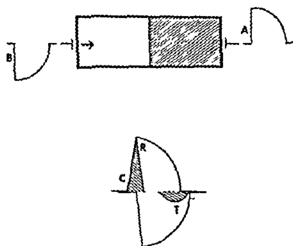


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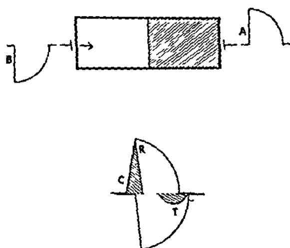


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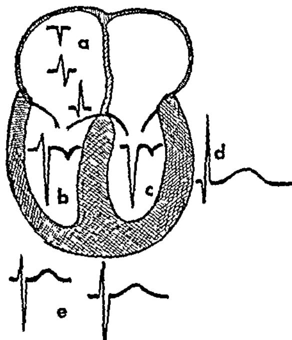


Fig 7 The intracardiac and extracardiac patterns according to the position of the electrodes (a) The auricular patterns are the same inside and outside changing only according to the position of the electrode (b) The right cavity pattern (c) The left cavity pattern (d) The left epicardial pattern (e) The right epicardial pattern (From Luisada *Heart Beat* New York Hoeber 1953)

(2) The ventricular complex recorded in *direct epicardial leads* is the result of activation of only the outer third of the ventricular wall (subepicardial layers)

(3) The gross sequence of ventricular activation is as follows

(a) Activation of the trabecular zone of the *direct epicardial leads* as a result of activation of the *intraventricular septum*

(b) Activation of the *anterior wall* of both ventricles(except the pulmonary conus) and of the posterior part of the right ventricle

(c) Activation of the *lateral wall* of both ventricles

(d) Activation of the *posterolateral wall* of the *left ventricle*

(e) Activation of the *pulmonary conus* and of the *lateral* and *basal portions of the left* ventricle

The final patterns of activation can be inscribed by using four electrodes two on the epicardium and two inside the ventricular cavities (Fig 7)

VOLUME CONDUCTOR—ELECTRIC FIELD

Any medium which permits the conduction of electrical current in three dimensions is called a *volume conductor* The human body because of its chemical constitution represents a volume conductor whose boundaries are limited by its surface However the conduction of the different tissues varies the highest being that of the heart and blood while the lowest is that of fat tissues For *practical reasons the changes of potential of* the human heart are usually recorded by electrodes placed on the surface of the body The *electrical phenomena caused by the heart can* be reproduced by immersing a battery in a large container of normal saline solution which is a homogeneous volume conductor If the *two poles of the battery are then connected* a current starts *to flow from the positive to the negative pole* through the conducting medium via an infinite number of pathways The greatest density of electrical charge travels through the shortest pathways between the

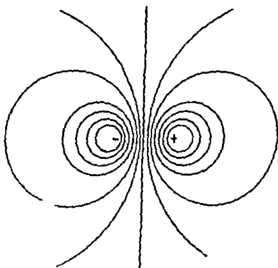


Fig 8 The electrical field of a battery The current flows from the positive (+) to the negative (−) pole through an infinite number of pathways indicated by the concentric lines (From Ashman and Hull *Essentials of Electrocardiography* New York MacMillan 1944)

two poles This constitutes the *electrical field* of the battery (Fig 8) The following principles are essential

(1) The difference of potential of the electric field diminishes as we move away from the source according to the law

$$EP = \frac{1}{d}$$

(E P = electric potential d = distance)

(2) The difference of potential has a maximum value at the poles and is zero in the central point between them

(3) The sum of all these intermediate points constitutes an electrical plane, perpendicular to the current of flow having zero potential Therefore any electrode placed on this plane will have zero potential and two electrodes placed on this plane will register no difference in potential

(4) Any electrode outside of this electrical field will have zero potential

The theory of unipolar leads is based on the above points

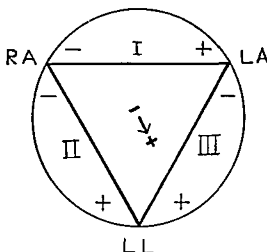


Fig 9 The Einthoven triangle with the heart in its center as a dipole The arrow represents the vector of the electromotive forces directed from the negative to the positive charges The sides of the triangle represent the three standard leads with their polarity The apices represent the three limb leads

EINTHOVEN'S HYPOTHESIS

According to this hypothesis Einthoven Fahr and De Waart described in 1913 *the three standard leads* They are supposed to represent the three sides of an *equilateral triangle* lying in the frontal plane of the body with its apices placed at the roots of the three extremities The heart is considered as a dipole lying in the center of this triangle with the positive and negative charges near each other This dipole actually represents the electromotive force of the heart (Fig 9) The body is considered as an homogeneous volume conductor of infinite area because the two poles of the dipole are very close compared to the extremely distant apices of the triangle

The above assumptions are not absolutely correct The triangle is *not* equilateral because of the irregular shape of the body the volume conductor is of *limited* volume and the human body is *not* a homogeneous conductor because of the different conductivity of the various tissues The existence of these errors has caused numerous discussions However the difference in tissue conduction is slight the dipole is at a great distance from the extremities and the asymmetry of the triangle is insignificant Therefore *this hypothesis is sufficiently accurate for clinical and experimental purposes* Einthoven himself was aware of the limitations of his hypothesis and stated "In regard to the equilateral triangle I assumed in the center of this triangle a dipole The triangle was supposed to be a homogeneous sheet of conducting material having an infinite extent in comparison with the minimal distance between the two points of the dipole The applicability of this scheme depends indeed on the fact that the electrodes are at a great distance from the heart If they are placed near the heart the errors are greater Even in the case of the limb leads the results cannot be absolutely correct

Einthoven Law

This law is true if the supposed triangle is equilateral and it states that *the algebraic sum of the variations of potential in leads I and III is equal to lead II* I + III = II The principle underlying this law is known as *Kirchhoff's 1st law* which states that the algebraic

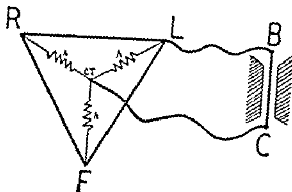


Fig. 10. The Central Terminal of Wilson
CT Central Terminal
C Central terminal electrode connected to the negative pole of the galvanometer
B Exploring electrode connected to the positive pole of the galvanometer and alternately to the point of the body (limb chest)
(From Sodi Pallares *New Bases of Electrocardiography* St Louis Mosby 1956)

sum of all differences of potential in a close circuit equals zero

Electrical Axis

In order to understand the meaning of the electrical axis it is necessary to define a few terms

(1) *Electromotive force* is the difference of potential of any electrical source expressed in volts

(2) *Vector* is a physical quantity having direction magnitude and sense and is represented by an arrow

(3) *Instantaneous electrical axis* is the momentary vector during any part of the cycle of the electrical activation of the heart

(4) *Mean electrical axis* is the average of all the instantaneous vectors and represents the mean electromotive force of depolarization or repolarization

(5) *Manifest electrical axis* is the projection of the mean electrical axis on the Einthoven triangle

During the electrical activation of the heart, many instantaneous vectors are created The average of these vectors constitutes the mean electrical axis The Einthoven hypothesis was of great help in the study and determination of the electrical axis The sense of this axis indicates the direction in which the current flows through the circuit The three sides of Einthoven's triangle are formed by the lines which connect the three limbs left arm and right arm (lead I) left leg and right arm (lead II) and left leg and left arm (lead III) The polarity of the three leads in relation to the galvanometer is shown in Fig 9 The three points in the center of the lines representing these leads have a zero potential The position of the electrical axis in reference to these leads is the angle of this vector to a line parallel to lead I which crosses the triangle in the middle (Fig 9) When this angle is 0 (in other words when the mean vector lies on lead I) the electrical axis is 0 if it points to the left or 180 degrees if it points to the right From this point on the electrical axis can have many positions Every position below this arbitrary line parallel to that of lead I will have a positive value while every position above this line will have a negative value

It has been accepted that values between 0 and +90 degrees constitute a *normal axis* between 0 and −90 a *deviation to the left* and between +90 and −150, a *deviation to the right* (Fig 11) Values between −150

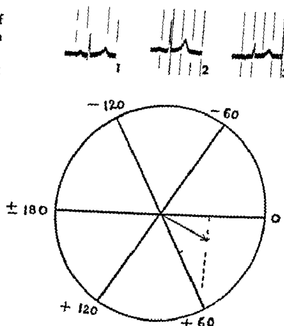


Fig 11 Determination of the electrical axis by the triaxial reference system of Bayley The axis of the above electrocardiogram is +26 degrees

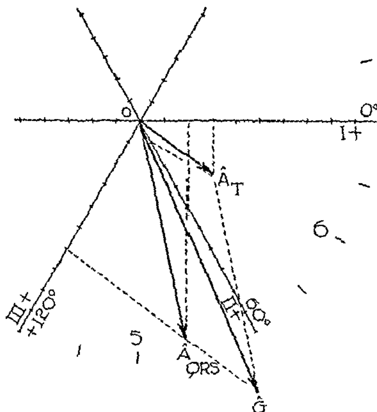


Fig 12 Determination of the ventricular gradient from the following values QRS in lead I = +2 units QRS in lead III = +6 units T in lead I = +3 units and T in lead III = +0 5 units Gradient *(G)* has a magnitude of 12 5 units and a *direction* of +65° (From Burch and Winsor A *Primer of Electrocardiography* Philadelphia Lea 195[illegible])

and −90 correspond to either an extreme right or an extreme left deviation (*reversed axis*)

The value of the electric axis is still controversial and is questioned by some authors There is no doubt that knowledge of the electrical axis is useful not only for a better understanding of Einthoven's hypothesis and the relationship of the various leads but also in the recognition of an atrial or ventricular preponderance Even though abnormal values of the electrical axis can be obtained from positional variations of the heart or conduction disturbances the usefulness of the electrical axis cannot be denied

DETERMINATION OF THE ELECTRIC AXIS

Either the *triangle* of Einthoven or the triaxial reference *system* of Bayley which is based on the Einthoven hypothesis can be used *for the determination of the electrical axis* In order to *determine* the electric axis of a tracing any *two* standard or limb leads can be used While the electric axis can be calculated for any *deflection* of the ECG (either P or QRS or T) we are usually interested in the *determination* of the axis of QRS If we wish to *determine* the *mean electric axis* we should measure the net areas under the positive and *negative* deflections of the QRS *complexes* This can be done with exactitude only by using a planimetric or electronic method and is *a time* consuming procedure Practically we can estimate these areas by *measuring the height* of the positive and negative deflections (*Q R* and S) from the baseline in leads *I* and III and obtaining the algebraic sum In the ECG of Figure *11* the positive deflection (R) is 9 mm the nega-

tive (Q) is 2 mm, and their algebraic sum is +7 mm in lead I In lead III, the positive deflection is 6 mm, the negative 0 5 mm, and the sum is +5 5 mm After calculation of these values, we can determine the mean axis by plotting them in the corresponding I and III leads of the triaxial system of Bayley or of the Einthoven triangle (arbitrary units can be used since we are not interested in the magnitude of the axis but only in its direction) Then, a perpendicular line is drawn through the plotted points on the lines of the leads; finally, a line is drawn from the center of the triaxial system (or the triangle) to the point of intersection of the two perpendicular lines This line represents the electric axis (Fig 11) For convenience, special charts have been made for the determination of the electric axis

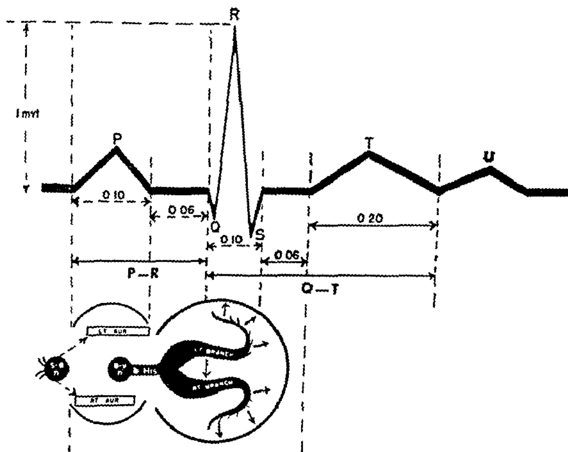


Fig 13 Duration and height of the various waves, segments and intervals in the normal electrocardiogram, with the direction of the stimulus through the various parts of the conducting system (From Luisada *Heart Beat* New York, Hoeber, 1953)

LEADS

According to the distance of the exploring electrode from the heart, there are three different types of leads direct, semi-direct, and distant

DIRECT LEADS

These can be used for the study of the epicardial or endocardial surfaces or points within the wall (during cardiac surgery) or

within the cavities of the heart (through cardiac catheterization) These leads are valuable because they allow exploration of small areas of the heart immediately underlying the electrode while the activity of the distant parts has only a minimal influence Actually the recorded deflection represents the *intrinsic deflection* of the explored section

SEMIDIRECT LEADS

These can be recorded when one electrode is very near the heart without being in contact with it The esophageal and bronchial leads and those using a thoracoscope touching the pericardium are examples of this type of leads The voltage of the recorded waves is already somewhat decreased by the distance between the exploring electrode and the heart

DISTANT LEADS

These are the leads which are of common use in clinical electrocardiography and will be discussed below The electrodes are placed either on the extremities or over the chest wall

According to the magnitude of the difference of potential between the two electrodes the leads are called *bipolar semi unipolar* or *unipolar* All of them can be *direct semidirect* or *distant* In the bipolar leads the difference of potential is caused by variations which have a similar magnitude at both electrodes In the unipolar the "distant" electrode is considered as having only negligible variation of potential In the semi unipolar the variations of potential of the "distant electrode are small but not negligible and have a definite influence on the tracing

BIPOLAR EXTREMITY LEADS OR STANDARD LEADS

These have been used since the early stages of electrocardiography They register the difference in potential between two points (extremities) and the lines connecting these points are the three sides of Einthoven's triangle Thus lead I registers the difference in potential between left arm and right arm Lead II registers the difference in potential between left leg and right arm Lead III registers the difference in potential between left leg and left arm In other words

I = LA RA
II = LL-RA
III = LL-LA

The polarity of these leads is such that in lead I the electrode of LA is connected with the positive pole of the galvanometer in leads II and III the electrode of LL is connected with the positive pole (Fig 9) This connection was suggested by Einthoven in order to obtain most positive deflections in the three leads and has been universally accepted These leads can be designated with Roman or Arabic numerals The usefulness of the above leads is considerable because they give the total picture of the variations of potential which reach the cardiac surface Moreover they have been used for a half century so that a great amount of empirical information has been accumulated with them Their limitations are due to the excessive distance from the heart and the fact that they register only those differences of potential which occur in the frontal plane of the body They are of complex interpretation because they represent the difference of potential between two points

SEMI UNIPOLAR LEADS

In these leads the changes of potential of the distant electrode are small even though not negligible The exploring electrode is placed over the precordium while the distant electrode is on one of the extremities For this reason they are designated as CR, CL, CF and according to the position of the precordial electrode the lead is called CR_2 CR_4 and so on (the electrode is placed in position 2 or 4—see below) None of these leads has proved completely satisfactory and for this reason they have become obsolete

UNIPOLAR LEADS

In the "unipolar" leads one electrode—called indifferent—is an artificial construction which is supposed to be exposed to minimal

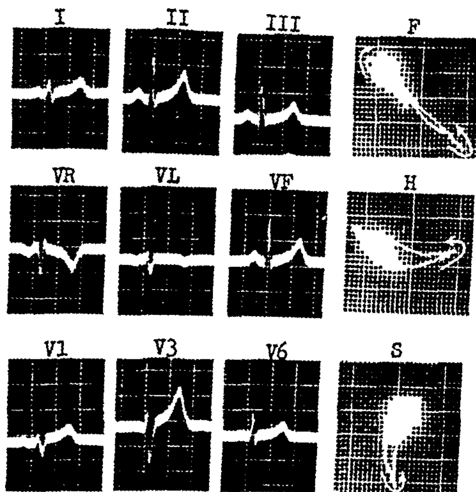


Fig 14 The n ~ ' ' ~ |
electrocardiogr m
of the cube (Fr
Mosby 1956)

or null variations of potential In order to achieve this the electrode could be put theoretically in a position which is perpendicular to the axis of the dipole but this is practically impossible It is possible to place it very far from the electric field of the heart This is actually done in the case of direct leads from the cardiac surface because the changes of potential of the latter are great in comparison with those of the extremities In the case of distant unipolar leads where the exploring electrode is relatively far from the heart and is exposed to smaller changes of potential this method is not satisfactory On the contrary Wilson s Central Terminal in which the indifferent electrode has negligible changes of potential gives satisfactory results

WILSON S CENTRAL TERMINAL—THE V LEADS

The central terminal is based on the fact that the sum of the changes of potential of the three extremities is supposed to be equal to zero in respect to any other point on the body surface Wilson connected the three electrodes of the extremities (LA LL RA) in one point which he called the *central terminal* If this point is connected with the negative pole of the galvanometer while another electrode is connected with the positive pole the variations of potential recorded will be only those reaching the exploring electrode The lead thus obtained is called V lead and can be considered from a practical clinical point of view

as a "unipolar" lead. The variations of potential which are recorded by this lead are about 30–40 times smaller than those recorded from the heart surface. Wilson introduced resistances of 5000 ohms in the three connecting wires in order to equalize the differences of potentials created between the extremities by different skin resistances. Theoretically the changes of potential of the central terminal are equal to zero or at least are very near zero.

Since the description of Wilson's central terminal many discussions have taken place and much experimental work has been done in order to confirm or exclude the exact contribution of the central terminal to the electrocardiogram recorded by a V lead. Since Einthoven's triangle is not equilateral, the theoretical basis for Wilson's terminal is actually missing. However, only small variations of potential are recorded by the central terminal (about 0.3 or less) and therefore the final tracing is only slightly modified by the currents of this terminal. Thus the central terminal lends itself to a satisfactory clinical use. The small magnitude of the changes of potential during the cardiac cycle was proven by Wilson by immersing a person in water and comparing the changes of potential in distal points of the water with those of the central terminal. Negligible differences were found.

GOLDBERGER MODIFICATION AUGMENTED V LEADS

The electrocardiogram recorded by means of the central terminal has usually small waves and is difficult to study. Goldberger suggested a modification consisting in the disconnection from the central terminal of the lead wire of that extremity whose potentials are recorded. With this method he obtained tracings which are 50% larger. He also omitted the use of the 5000 ohms resistor because he thought that they had no significant influence in balancing the skin resistances. He called these leads *augmented unipolar leads* (aV leads: aVR, aVL, aVF). Several subsequent studies pointed out that Goldberger's leads present several inherent inaccuracies mostly due to inequality of skin resistances. Present day technique embodies the best features of Wilson's terminal (including the resistances of 5000 ohms) while it provides for alternate disconnection of the central terminal from the limb under study. Connection of the three wires with the central terminal and disconnection of the wire from the limb under study is automatically obtained in most modern apparatus where the *lead selector* is successively placed in positions aVR, aVL, and aVF.

The advantages of the unipolar extremities leads are the following: (1) they give a better idea of the electrical events of either the epicardial or the cavity surfaces; (2) they help in the determination of the electrical position of the heart; (3) they are useful in the diagnosis of localized infarctions: the high lateral infarct is recognized through observation of aVL while the postero-diaphragmatic infarct is well revealed by aVF; (4) from these leads we can explain the patterns of the standard leads.

The following equations allow the calculation of the standard leads from the V leads or vice versa:

$$VL = \frac{I - III}{3}$$ or for the augmented lead

$$aVL = \frac{3VL}{2}$$

$$VF = \frac{II + III}{3}$$ and for the augmented lead

$$aVF = \frac{II + III}{2}$$

$$VR = \frac{I + II}{3}$$ or for the augmented lead

$$aVR = \frac{-(I + II)}{2}$$

PRECORDIAL V LEADS

The limitations of the bipolar and unipolar leads was recognized early in electrocardiography. The precordial leads were studied in order to explore the various areas of the heart. They give tracings which are remarkably similar to those obtained by means of

direct leads although not identical. This was proven by animal experiments and by direct tracings in occasion of cardiac surgery. Due to their proximity to the heart they have waves of great amplitude.

The above described semi-unipolar leads were first employed but were subsequently abandoned because of various limitations. The use of the Wilson central terminal removed these difficulties. With the central terminal as an indifferent electrode and an exploring electrode subsequently placed over different points of the precordium we can record the precordial "unipolar" leads or precordial V leads (V refers to the central terminal). According to the position of the chest electrode the lead is called as follows:

V_1 The electrode is over the 4th right intercostal space near the sternum.

V_2 The electrode is over the 4th left intercostal space near the sternum.

V_3 The electrode is half way between points 2 and 4.

V_4 The electrode is over the 5th left intercostal space on the midclavicular line.

V_5 The electrode is on the horizontal level of V_4 but on the anterior axillary line.

V_6 The electrode is on the horizontal level of V_4 but on the midaxillary line.

These are the six most commonly used precordial leads. In addition several other leads can be employed in order to explore the posterior surface of the chest or other points above or below the conventional.

The following four points are used in several cases:

V_7 The electrode is on the horizontal level of V_4 but on the posterior axillary line.

V_8 The electrode is on the horizontal level of V_4 but on the angle of the left scapula.

V_3R and V_4R are points located on the right side of the chest in positions which are symmetrical with those of 3 and 4.

V_E The electrode is placed over the xiphoid process.

Points one or two intercostal spaces *above* or *below* the conventional ones are designated with the same symbols adding plus or minus numerals like $V_1{}^{+1}$, $V_1{}^{+2}$ or $V_1{}^{-1}$, $V_1{}^{-2}$.

The general electrocardiographic pattern of the precordial leads is such that as the exploring electrode moves from right to left the R waves become taller and the S waves become smaller. The deepest S wave is usually in V_1, V_2 while the tallest R is in V_4, V_5.

The pattern rS or RS recorded in V_1, V_2 is a typical *right ventricular pattern*. The first positive deflection is due to activation of both the ventricular septum (vector left-to-right) and of the trabecular zone of the right ventricular wall (vector from endocardium to epicardium toward the electrode). The subsequent S wave is due to a vector from endocardium to epicardium in both ventricles, chiefly the left.

The pattern qR recorded in V_4, V_5 is a typical *left ventricular pattern*. The first negative deflection is due to activation of the septum (vector from left to right away from the electrode). The subsequent R wave is due to activation of the left ventricular wall (vector from endocardium to epicardium toward the electrode).

At some point between V_3 and V_4 the pattern is that of a rather large diphasic or polyphasic wave (RS or RSr). This point is called "the transitional zone" because the electrode registers currents from the anterior surface of the i.v. septum, i.e., from both ventricles.

The advantages of the precordial leads are: (1) they record the variations of potential which take place in the points underlying the exploring electrode because of the small solid angle which they have;* (2) they record phenomena in a horizontal plane; (3) the intrinsic deflection is more accurately measured so that detection of ventricular hypertrophy is easier; (4) they give a clear picture of the preponderance of one of the ventricles, and they are very helpful in the diagnosis of interoseptal infarction and bundle branch block.

ESOPHAGEAL V LEADS

Exploration of the posterior wall of the heart may be needed in certain cases. This

* *Solid angle* is an imaginary cone with its apex on the exploring electrode and its base on the myocardium. As the electrode moves farther from the heart the base of the cone becomes larger and the surface from which potentials are recorded becomes greater.

can be done by using the central terminal (indifferent electrode) and an esophageal electrode (exploring electrode) The latter consists of an insulated wire with an electrode at the tip it is passed through the nose to the pharynx and down the esophagus The registration of the electrical phenomena is obtained at two levels i e at 50 to 60 cm from the nostrils (posterior surface of the left ventricle) and at 30 to 40 cm (posterior surface of the left atrium) These leads have as a prefix the letter E followed by the distance in cm (E_{40} or E_{50} and so on) They are not in common clinical use because of the technical difficulties and the limited information which they give They may be useful in the diagnosis of certain arrhythmias atrial enlargement small recent posterior infarctions and localized conduction disturbances (atrial or ventricular)

THE NORMAL ELECTROCARDIOGRAM

The electrocardiogram is usually recorded on a 6 cm wide film at a conventional speed of 25 mm *per second* Special studies may require records taken at different speeds or on a different film Vertical and horizontal lines are inscribed on the film The vertical lines are employed for measuring the time intervals between the different waves the distance between the thin lines is 0 04 second that between thick lines is 0 20 second The horizontal lines are used for the measurement of the amplitude of the waves they are 1 mm from each other

Einthoven arbitrarily used the letters P Q R S T and U as designations for the various *waves* The six letters represent the positive and negative peaks of three main deflections P QRS and T plus the small and inconstant U wave It is now known that *P wave* represents the activation of the atria *QRS* the activation of the ventricles and *T* the repolarization of the ventricles In regard to the *U wave* there is still lack of agreement according to one group it represents the repolarization of the intraventricular septum and papillary muscles while according to another it is a wave of afterpotential By convention *Q* is the first negative peak of the ventricular complex *R* the first positive peak (whether or not there is a Q) and S the first negative peak after R If more peaks are present they are designated as R S R′ S′ etc Whenever the whole ventricular complex is represented by a negative wave this is called a *QS wave* On the other hand both P and T refer respectively to the atrial complex and to the final ventricular wave irrespective of whether they are positive or negative

Between the six waves of the ECG are *segments* which represent the parts between the waves and *intervals* which include the segments plus one or more waves Although normal variations cause differences between the electrocardiograms of normal people *mean values* have been established from thousands of measurements in normal people The measurements usually are taken in the standard leads because they are more stable

P WAVE

This wave represents the activation of the atrial walls Its duration normally should not exceed 0 10 seconds and its height should not be greater than 2 5 mm

P R INTERVAL

It is the distance from the beginning of P the beginning of Q or in the absence of this represents the time elapsed from the initiation of the impulse in the S A node to the beginning of ventricular activation The upper normal limit for adults is 0 22 seconds In children this interval should be shorter according to the age and the heart rate

P R SEGMENT

It is the distance between the end of P and the beginning of Q or in the absence of this of the R wave The Ta wave (a negative wave due to repolarization of the atria) is usually hidden within this segment or during

the following QRS complex A depression of P R may be due to changes of the P Ta segment or to an early Ta

QRS COMPLEX

This complex represents the depolarization of the ventricles Its duration should not exceed 0 10 seconds and its amplitude should not be greater than 25 mm or smaller than 5 mm

S T SEGMENT

It is the part between the end of the QRS and the beginning of the T wave and it varies in duration from 0 05 to 0 15 second The point of junction between QRS and S T is known as point J (junction) and should be isoelectric

S-T INTERVAL

It represents the duration from the end of the QRS to the end of the T wave

T WAVE

It represents the repolarization of the ventricles and varies in duration and amplitude

It may have different polarity in different leads It is normally negative in the chest leads of normal children not of infants

Q T INTERVAL

It is the interval from the beginning of Q to the end of the T wave It represents the duration of "*electrical systole*" and varies with the age and sex and especially with the cardiac rate Its normal values can be found on the base of special formulas Bazett s formula is $Q\,T = K \sqrt{R\,R}$ where K (a constant) is 0 40 for women and 0 38 for men

U WAVE

It is a small positive wave following the T wave it is inconstant and of unknown significance (Fig 13)

ANATOMICAL AND ELECTRICAL POSITION OF THE HEART

The anatomical position of the heart within the chest depends greatly on the age and the body shape of the subject Tall slender individuals have a heart which is in a more vertical position on the contrary short squat individuals have a heart in a more horizontal position A rise of the diaphragm greatly influences the position of the heart causing it to become more horizontal This occurs in pregnancy ascites and obese persons with a large abdomen X ray examination usually gives a good idea of the anatomical position of the heart In many cases the anatomical position corresponds to the electrical position of the heart However in certain cases no such correspondence is found

In order to study these different positions of the heart one should keep in mind that the heart may rotate around three main axes the anteroposterior the longitudinal and the transverse

Rotation around the anteroposterior axis in a counterclockwise direction brings the heart to a horizontal position while rotation *in a clockwise direction* brings it to a vertical position

Rotation around the longitudinal axis in a clockwise direction brings the right ventricle more to the left while *rotation in a counter clockwise direction* brings the left ventricle more to the right According to the degree of rotation there may be slight moderate and marked clockwise or counterclockwise rotations The position of the *transitional zone* in the precordial ECG determines the degree of either rotation

Rotation around the transverse axis brings the apex forwards or backwards

It should be kept in mind that rotations around more than one axis frequently occur For example a horizontal heart frequently presents a counterclockwise rotation around

its longitudinal axis, plus displacement of the apex on account of rotation around the transverse axis.

Electrical Position

The electrical position of the heart can be established from the ECG patterns of the V limb leads and especially VL and VF. Since the relative spatial positions of the two ventricles influence these leads, the relationship between the precordial patterns and these leads has been used for determining the electrical position of the heart by Wilson and his associates. According to them the following six electrical positions are possible.

(1) *Horizontal position*: the pattern of VL resembles that of V_6 (left ventricle) while that of VF resembles V_1 or V_2 (right ventricle).

(2) *Semihorizontal position*: the pattern of VL resembles that of V_6 (left ventricle) while VF has a small complex.

(3) *Vertical position*: the pattern of VL resembles that of V_1 or V_2 (right ventricle) while the pattern of VF resembles that of V_6 (left ventricle).

(4) *Semivertical position*: the pattern of VL resembles that of V_1 or V_2 (right ventricle) while VF has a small complex.

(5) *Intermediate position*: the patterns of VL and VF are similar and resemble that of V_6 (left ventricle).

(6) *Undeterminate position*: there is no obvious relationship between the precordial and the limb leads.

THE VENTRICULAR GRADIENT

The importance of the ventricular gradient was stressed by Wilson and his co-workers. It was neglected for several years until its importance was brought out again by Ashman and Byley. Ashman states that the gradient is an expression of those electrical forces which appear when the sequence of repolarization differs from the sequence of depolarization.

When the two processes of depolarization and repolarization proceed in the same direction and have the same rapidity, as in certain experimental conditions, the algebraic sum of the areas enclosed under the waves QRS and T equals zero. In such a case *there is no ventricular gradient*. On the contrary, if the processes of depolarization and repolarization proceed in an opposite direction or have a different speed, then the enclosed areas under the QRS and T are not equal to zero.

The normal human electrocardiogram always has a ventricular gradient. The reason for this is that the repolarization of the subendocardial areas is somewhat slower than that of the subepicardial layers. As a result repolarization starts in the subepicardial layers and proceeds toward the endocardium with a vector directed inwards. For this reason the ECG recorded on the heart of a normal adult has a positive T wave. On the contrary, hearts of small mammalians normally have a negative T wave in both direct and precordial leads (the vector of repolarization is directed outwards; the reasons for this fact are still under discussion).

The absence of a ventricular gradient in the ECG is always an abnormal phenomenon. The entire process of depolarization can be indicated by a vector which represents *the mean electric axis of QRS* and which is designated as AQRS (the arrowhead indicates the vectorial quality). In the same way the entire process of repolarization can be indicated by a vector which represents *the mean axis of T* and which is designated as AT. The vector representing the algebraic summation of the two is designated as G (gradient). These vectors can be used in order to demonstrate that the recovery process has a different direction from the activation process.

PRIMARY AND SECONDARY T CHANGES

The clinical importance of the ventricular gradient is its application to the differential diagnosis of the *primary T changes* from the *secondary T changes*. The secondary changes are usually *not* caused by myocardial damage but are the result of changes of QRS. Examples are represented by the ventricular extrasystoles and the right and left bundle

branch blocks, where considerable changes in the area of the QRS are followed by opposite changes of the area of T On the contrary, in primary changes of T, the QRS is not altered This means that there is a primary disturbance in the recovery process which is responsible for the T changes Ischemia of the myocardium and the changes which follow digitalization are examples of primary T changes

The relationship of the values ÂQRS, ÂT and G is revealed by the following formulae $\hat{G} = \hat{A}QRS + \hat{A}T$ and $\hat{A}T = \hat{G} - \hat{A}QRS$

DETERMINATION OF THE VENTRICULAR GRADIENT

The most accurate method for measuring the ventricular gradient is planimetric but is not practical A more simple method is to estimate the areas of the waves above and below the isoelectric line by multiplying their durations at the base by one-half of their height (these waves are roughly triangular) After obtaining the algebraic sum of QRS and T in two leads (preferably I and III), we find the ÂQRS and the ÂT by plotting these values on the Bayley triaxial reference system or on the Einthoven triangle By further drawing a parallelogram of vectors, we can determine the position and magnitude of the ventricular gradient (Fig 12) The extreme normal values for the position of the gradient are between −17 and +86 degrees, and the extreme normal values for the magnitude are between 3 5 and 23 Ashman units with an average of 13 units * The most important clinical application of the ventricular gradient is in the interpretation of T wave changes both in normal and abnormal conditions Other factors which influence the gradient are heart rate, age, rotation of the heart (particularly around the longitudinal axis), postural changes, exertion food intake, and probably others Because of these factors and of the fact that occasionally both primary and secondary changes of the T may occur in the same patient, many authors attribute more importance to the morphology and shape of the T than to the gradient In spite of these limitations, it should be stated that the ventricular gradient is of definite value in the differential diagnosis between primary and secondary T changes

VECTORCARDIOGRAPHY

Mann, in 1920, constructed manually a vectorcardiogram from the electrocardiogram and called it "monocardiogram" This method was ignored until Wilson revived the interest *by using a cathode-ray oscilloscope, and called* the method "vectorcardiography

Although general information about the form of the vectorcardiogram (VCG) can be obtained from the electrocardiogram and vice versa, there are differences in data obtained from the two methods The ECG represents scalar quantities, the VCG, vector quantities The last can be derived from the first, but r represent only grossly approximate val comparison with those obtained through of the cathode ray tube The best me however, is to obtain the VCG photog cally through the use of a cathode ray osc scope with amplifiers (Fig 14) Alt there is general ag that study of electrical events o in planes oth than the frontal is profitable, there is no agreement in regard to placement of the electrodes Several systems for the placement have been proposed in order to obtain the spatial VCG (cubic, rectangular, tetrahedral, etc), but the application of any geometric frame to the human body necessitates certain assumptions which are not always correct Since no planar or spatial system can be applied to the body without intrinsic error, the choice must be based on other considerations

The equilateral of Wilson seems to be the best The s one additional etrode placed in which is differ- from those at ved for the ard limb le trode is placed

magnitude l in
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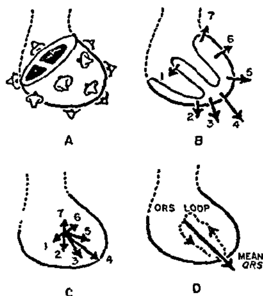


Fig 15 The QRS vectors of the heart (A) Early QRS vector is directed perpendicularly to the surface of the region where it is generated The T vectors have a similar direction in the normal subject (B) Frontal plane cross section of the heart illustrating the magnitude direction and effective source of resultant QRS vectors from instant to instant during a single QRS cycle (C) The instantaneous vectors from the previous figure are drawn as if they all originated at the same point, the relative zero point of the electrical field in the frontal plane (D) The pathway of the termini of the QRS vectors is a loop (QRS loop) projected to the frontal plane of the body (From Grant *Spatial Vectorcardiography* Philadelphia Blakiston 1951)

on the back of the thorax 3 cm to the left of the spinous process of the 7th vertebra

Although the configuration and orientation of the spatial VCG differs for each system and for the normal and abnormal states a description of the spatial VCG will be of value As stated earlier the electrical forces generated during the activation of the heart can be represented by vectors These vectors generated at every moment have different magnitude and direction and radiate perpendicularly to the heart surface The change in location of the resultant vector from instant to instant reflects the fact that these electrical phenomena start at one point and spread from an area to another within the heart Since the heart is a volume structure and the body a volume conductor all these vectors have a three-dimensional orientation which is recorded in three planes the frontal the horizontal and the sagittal A vector for a given instant during the P QRS or S T cycles is called *an instantaneous vector* and the average direction and magnitude of all these instantaneous vectors is called *the mean vector* The termini of all these instantaneous vectors describe a "loop" which is the vectorcardiogram (Fig 15) The symbolic representation of these loops in sEP sEQRS sET loop (s means spatial Γ indicates electric quantity of vectorial nature) The magnitude and spatial direction of these loops is determined by the order of depolarization and repolarization of the atria and ventricles and by the state of the myocardium Since variations in the state of the myocardium alter the order of depolarization and repolarization by modifying the magnitude and orientation of the vectors the study of *the spatial VCG* is of clinical importance The VCG provides information of considerable value for understanding the fundamental principles of the electrical events associated with the heart It is likely that valuable data will eventually be supplied by the VCG which will supplement the ECG

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CHAPTER 28

Arterial Hypertension

C A McKinlay, M D

I. INTRODUCTION

ARTERIAL hypertension and associated cardiovascular renal disease have become the chief causes of death in this country and therefore present a serious challenge to medicine Although there are many disease states in which arterial hypertension appears, so-called essential or primary hypertension of unknown etiology is by far the most frequent The most common of known associated conditions are Bright s disease and pyelonephritis which, although infrequently found should always be considered in diagnosis To facilitate consideration of the uncommon causes of hypertension, Page, in his classification of arterial hypertension (TABLE I) has grouped the various clinical types under five headings —renal cardiovascular, cerebral, endocrine and unknown

TABLE I

CLASSIFICATION OF ARTERIAL HYPERTENSION

Renal
- a) *Affections of Vessels*
  - Arteriosclerosis
  - Panarteritis nodosa
  - Arteritis
  - Anomaly
  - Obstruction (tumors aneurysm, arteriosclerosis embolism, thrombosis)
  - Thromboangitis obliterans
  - Visceral lupus erythematosis
  - Scleroderma
- b) *Affections of Parenchyma*
  - Acute nephritis
  - Chronic nephritis
  - Pyelonephritis
  - Hydronephrosis
  - Polycystic disease
  - Amyloidosis
  - Infarcts
  - Tumors
  - Hypernephroma
  - Ectopia
  - Toxemia of Pregnancy
  - X ray Lesions
  - Renal stones
  - Hypogenesis
  - Dystopia
- c) *Affections of Perinephric Structures*
  - Perinephritis
  - Tumors
  - Hematoma
  - Retroperitoneal masses causing pressure on parenchyma
  - Wilms Tumors
- d) *Affections of Ureter*
  - Obstruction (pelvis ureter, prostate)
  - Pyelitis

Cerebral
- Increased intracranial pressure (trauma, tumor, inflammation)
- Diencephalic stimulation
- Anxiety states
- Lesions of brain stem (ascending paralysis, poliomyelitis)
- Acute porphyria

Cardiovascular
- Heart failure
- Arterio-venous fistulae
- Heart block
- Coarctation of aorta
- Atheromatosis (systolic hypertension)
- Lead poisoning ?
- Polycythemia

Endocrine
- Chorionepithelioma
- Pheochromocytoma
- Paraganglioma (organ of Zuckerkandl)
- Adrenal carcinoma
- *Adrenal hyperplasia ?*
- Cushing s syndrome (pituitary adenoma)
- Pituitary basophilism ?
- Acromegaly
- Thymic carcinoma
- Hyperthyroidism
- Arrhenoblastoma

Unknown
- Essential hypertension
- Malignant hypertension

Although infrequent and sometimes obscure causes are difficult to establish they must not be overlooked because they may possibly be remedied

For the purposes of this article attention will be limited specifically to essential or primary hypertension and sequelae

II PRIMARY HYPERTENSION

DEFINITION

Primary or essential hypertension may be defined as elevation without known cause of the blood pressure above a certain level empirically established by examinations of presumably normal people No level has been universally accepted but *blood pressure above 140/90 or 145/90 has often been con*sidered abnormal Master and others have considered a higher standard of normal

Perera states that there is considerable evidence to support the view that pressure of 90 *diastolic should be regarded* with suspicion and that hypertension should be defined as the repeated finding of a casual diastolic pressure of 90 mm Hg or more not including however persons with transient rises those with marked obesity (unless values are in excess of 105) and those with possible arterio*sclerotic causes (unless values are in excess* of 100)

III ETIOLOGY

Although once its true etiology is known hypertension ceases to be classified as primary specific characteristics of the course of hypertension in certain types of individuals have become apparent The relatively good toleration of hypertension by many obese women some of whom have an emotionally labile component is generally accepted Trigger mechanisms which are not causative stand out and *include emotional strain anxiety unre*solved conflicts and if you will have it the pressure and tempo of modern living and going It seems established that individuals from primitive civilizations usually do not have primary hypertension except when transplanted to so called modern living conditions

The hereditary factor has long been considered in essential or primary hypertension ckering states that it would seem justifiable conclude that the environmental factors are more importance than the hereditary factors in the pathogenesis of hypertension This observer considers the rejection of the concept of essential hypertension as a specific entity and would define hypertensives as that group of the population with arterial blood pressure exceeding an arbitrarily selected value in whom no specific cause for high pressure can be detected The factors of age sex and inheritance can be defined approximately The influence of environmental factors which would seem by exclusion to be of great im*portance remains to be explored*

Clinical study may embrace some of the environmental factors better than animal experimentation For in addition to fundamental biochemical studies of lipid metabolism estimation of the sum total of the numerous nervous and emotional factors that characterize *the life* of modern man *should yield* important information

IV CLINICAL FEATURES

1 VARIATIONS IN NORMAL INDIVIDUALS

The fact that blood pressure is variable to some extent in normal individuals dictates evaluation of those factors that may give temporary physiologic aberrations It is known that emotions muscular effort and meals tend to increase blood pressure and that sleep in

fections and inanition tend to lower it. Assumption of upright posture is said to cause an immediate fall of systolic blood pressure which may soon be regained. The blood pressure rises gradually during the day. Clinical experience teaches the examiner to establish the patient's blood pressure for the given observation by, if necessary, repeated readings until the lowest sustained record is obtained. Sometimes a truer level of the individual's blood pressure is obtained by observation on a later day.

2 VASOMOTOR LABILITY

In this stage of primary hypertension there is a tendency for the blood pressure to be periodically rather than constantly elevated above normal. The cold pressor test has had some use in attempting to establish the prehypertension stage. Periods of elevation increase in duration and may go on to the phase of fixed hypertension. Not all cases progress to sustained hypertension and even in the so called fixed stage there is often considerable lability of blood pressure. Study of young adults with labile hypertension shows that they tend to develop fixed hypertension more frequently than those with normal blood pressure.

3 POSSIBLE SYMPTOMS AS RELATED TO PATHOLOGY

There is no symptom complex common to primary hypertension. While in individual cases change may be associated with symptoms referred to the nervous system such as hyper excitability and to vasomotor disturbances, in others renal and retinal arteriolar sclerosis appears with varying degrees of damage. Thus it may be that headaches, nervousness and vertigo predominate in certain individuals more as an index to their reactivity than to specific effects of the hypertension. Likewise cardiac arrhythmias may appear as evidence of irritable myocardium before cardiac hypertrophy appears due to arteriosclerosis. Sometimes combinations of symptoms appear. Visual changes related to alteration of the retinal arterioles with hemorrhage and exudate are sometimes the initial warning of hypertension and the concomitant malignant or arteriolar change that may occur.

4 MALIGNANT HYPERTENSION

So called malignant hypertension has been ushered in by retinal impairment before renal impairment and/or insufficiency or uremia intervened. In other cases malignant hypertension may be looked upon as an accelerated phase of disease of which one end result is ultimately uremia. However, developing cerebral or cardiac damage may determine the final chapter in the disease through major extension of the arteriosclerotic process to the coronary or cerebral vessels whichever the case may be. The viewpoint is held by Perera that the sometimes abrupt shift and acceleration of the process from the arteriosclerotic to the arteriolar with retinal and renal damage represents a qualitative change.

In the estimation of prognoses experience has emphasized that high and fixed resting diastolic pressure augurs less well for the patient than the labile variety.

The question arises whether arteriosclerosis precedes hypertension or whether it is a result of it. Page states that most evidence suggests but does not prove that hypertension may be initiated in the absence of renal arteriosclerosis as demonstrated by the usual methods of pathology. That the kidneys participate in hypertension was shown experimentally by Goldblatt and others who produced persistent elevation of systolic blood pressure by means of induced renal ischemia.

Obesity and Hypertension in a Woman

Twenty-eight years previously an obese 57 year old housewife appeared in the office because

blood cholesterol 187 mg per cent. During the

sustained. Ten years after first observation the

blood pressure was 212/130 the weight was 200 pounds Blood pressure levels tended to be somewhat higher in spite of current therapeutic attempts Fifteen years after first observation there was elevations of systolic levels to 200 or over and of diastolic levels to over 100 Twenty-one years after first observation blood pressures of the order of 244/144 were obtained 1 year later readings of 300/158 and 288/140 were found Three years later blood pressures of 288/148 were recorded and during the last 3 years of observation readings of 300/164 and 260/156 were obtained the latter at age 85 when her weight was 184 pounds No evidence of malignant hypertension had developed There had been one or two instances of syncope and vertigo but no major cardiovascular episode had occurred The patient was last observed at age 85

This case is recited because it illustrates how well essential hypertension may be tolerated by certain obese women This fact fits in with the relative infrequency of coronary disease manifested during menstrual life and afterward the increased frequency tending to approximate that in men The possibility of hormonal effects must be studied further experimentally and clinically

V MEDICAL TREATMENT

1 GENERAL FEATURES

Treatment must be individualized it depends in large measure upon the recognition of exciting and aggravating factors and upon appreciation of the individual's reactivity and level of emotional response Thorough understanding of the patient should form the basis of sound estimation of treatment and the relative values of drug therapy or abstinence therefrom Useless or questionable therapy in marginal cases may lead to undue and imaginative fears Headaches may occur in over one half of hypertensives and when they do not respond to simple measures may be benefited by anti hypertensive drugs As a rule symptom free hypertension may well be let alone except when its degree is sufficient in itself to indicate increased hazard of unreasonable strain upon the cardiovascular system The reassurance of some patients with auxiliary treatment and mild sedation may keep a fair per cent of these individuals from the need for major therapeutic attempts for appreciable periods of time

2 DRUG THERAPY

The use of drugs in primary hypertension has had increased impetus since the introduction of the Rauwolfia alkaloids These compounds are usually safe but may produce mental depression Ergot derivatives have not given sustained effects and may provoke nausea and vomiting

3 GANGLIONIC BLOCKING AGENTS

Ganglionic blocking agents such as the hexamethonium compounds and petolinium may modify some of the accelerated stages of primary hypertension but frequent titration and unfavorable side effects limit their application In 30 consecutive patients with azotemia Perera found that pentolinium in doses sufficient to lower blood pressure to normal or near normal levels failed to improve the renal insufficiency Few patients could be maintained for long periods on drugs

Combined therapy has been reported by Moser *et al* who conclude that the over all percentage of patients considered to have had a good or excellent response to pentolinium or mecamyl amine (inversine) therapy in combination with reserpine and/or hydralazine (apresoline) was 65%

Ford and others studied the pharmacologic effects of inversine and found that its effects are its prompt onset and long duration and believe that inversine is the drug of choice in the treatment of patients with moderate to severe hypertension

VI SURGICAL TREATMENT

1 SYMPATHECTOMY

Sympathectomy has limitations of usefulness especially in the presence of marked renal damage However survival figures (Perera) indicate that about 50% of the patients in the accelerated stage who qualified

for operation lived for a period close to 5 years As ganglionic blockers have been used for only 4 or 5 years accurate comparison with surgery is not possible

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CHAPTER 29

Hypertensive Heart Disease

C A McKinlay MD

I INTRODUCTION

Cardiovascular disease has become captain of the forces of death and therefore emphasizes hypertensive heart disease as the most frequent cardiopathy. Primary or essential hypertension and the frequent sequence of heart disease will be considered as a clinical entity and although the cause remains unknown provocative factors will be discussed

II PATHOLOGIC CONSIDERATIONS

1 PRIMARY OR ESSENTIAL HYPERTENSION

This condition has been discussed elsewhere *in this book* and is now identified again as hypertension of unknown etiology tending to run a course with cardiac cerebral and less often renal complications which themselves tend to define the clinical syndrome. There are many disease states with hypertension that might lead to the same course of events as those that follow essential hypertension. However the latter surpasses by far other causes of hypertensive heart disease and hence its relative importance. If it is accepted that due to some unknown cause hypertonicity of arterioles occurs and hypertension results only a mechanism is described. The mechanism for the production of hypertensive heart disease appears to be one of overwork. This assumption taken alone may be over simplification in view of the concomitant arteriosclerotic changes that develop and which themselves modify the process. It is felt that hypertension precedes the arteriosclerosis. With the inevitable progression of arteriosclerosis with hyperplasia and hypertrophy of the vessel walls there is the continued strain of hypertension augmenting fibrinoid degeneration and atheromatous formation

The evolution or acceleration of primary hypertension to the malignant form is an occasional development with papilledema retinal hemorrhages and retinal exudates as chief characteristics arising from wide spread necrotizing arteriolitis. The kidneys also participate in retrogression with proteinuria hematuria and impaired function. The heart is far more frequently significantly involved than the kidneys

2 CARDIAC HYPERTROPHY

The cardiac response to increased work load of essential hypertension is hypertrophy of the left ventricle probably preceded with some degree of dilatation. The early stages of compensatory hypertrophy are not measurable by present clinical methods. Increased work demands are followed by recurrence of dilatation and possibly by further hypertrophy. However with later inability of the left heart to accomplish its work there is increased pressure within the left auricle and then within the pulmonary veins. Pulmonary stasis occurs later with increased work of the right ventricle and with dilatation hypertrophy, and increased pressure in the right auricle and congestion of the liver splanchnic area and systemic veins as failure occurs

At autopsy the hypertrophied heart weighs 500 or more gm the valves are often normal

the myocardium may show areas of fibrosis (less often diffuse distribution) and the coronary arteries show sclerosis in most instances In congestive heart failure the most frequent mode of death usually all of the chambers of the heart are dilated and hypertrophied The myocardium is definitely thickened

The incidence of coronary sclerosis in primary hypertension is high Bell and Clawson found notable change in 90% of hypertensive hearts it has been stated by Nadler that about 15% of deaths from hypertension are directly due to coronary disease

III CLINICAL FEATURES

1 EARLY LEFT VENTRICULAR STRAIN

In the stage of left ventricular strain before decompensation has occurred there are few if any disturbances of cardiac function At this period myocardial irritability sometimes is present and is indicated by attacks of paroxysmal tachycardia sinus tachycardia and premature contractions Major arrhythmias including auricular fibrillation and heart block have usually not transpired in early and latent stages Subjectively headaches fatigability and nervousness may appear at this stage and may or may not be related directly to cardiac overload The electrocardiogram may be normal or show progressive changes left axis deviation S T depression and sometimes T wave negativity in leads 1 V 5 and V 6 Evidence of left ventricular strain is usually although not always present at the time of the first decompensation Auricular fibrillation not infrequently supervenes although sinus rhythm may persist throughout the course Various degrees of heartblock are not uncommon and have variable prognostic import with that of complete block the most severe There may be influence upon the electrocardiogram due to the degree of development of coronary arteriosclerosis and insufficiency

2 BEGINNING CARDIAC DECOMPENSATION

From clinical experience one is struck with the frequency with which acute respiratory tract infection initiates the first bout of decompensation as well as recurrences It is also recognized that cardiac decompensation may predispose to respiratory tract infection It is possible that the demands of the hypertrophied left ventricle for nutrition extend beyond the capacity of the coronary circulation and give rise to relative coronary insufficiency Angina pectoris has often been present for appreciable periods of time Electrocardiographic changes showing various stages of ischemia appear later with damage and necrosis of myocardial infarction

Cardiac decompensation may follow sudden strain and excitement or unusual effort which is beyond the individual s customary physical habits Or the attack may without prodroma appear at night and waken the patient with intense dyspnea and cough rusty sputum sometimes hemoptysis and rales at the lung bases There is usually some degree of cyanosis The lung bases particularly show moist rales and there is usually an apical systolic murmur over the apex and precordium A diastolic murmur is less common Advanced cases with marked arteriosclerosis of the aorta may have systolic and diastolic murmurs of aortic stenosis and insufficiency

3 CARDIAC HYPERTROPHY

Although slight and early dilatation and hypertrophy of the left ventricle cannot be demonstrated by present clinical methods usually by the time decompensation has occurred the heart is demonstrably enlarged The apex is displaced to the left and downward The 6 foot film has very definite value in determining the cardiac border and particularly rounding of the left ventricle which may extend below the diaphragm The prediction tables from measurements of the teleo-

roentgenograms published by Ungerleider and Gubner are valuable and simple in application. The x-ray film also has value in determining pulmonary stasis.

IV. DIFFERENTIAL DIAGNOSIS

Other forms of heart disease may be associated with essential hypertension, such as that of rheumatic and syphilitic origin. Here the degree of hypertension may act as a separate factor having sometimes little or great influence as the case may be upon the course of the primary disease. Coronary arteriosclerosis may have transient periods of hypertension that may lead to misinterpretation. The secondary hypertension of renal disease and of polycystic disease and of endocrine disturbance is usually established by characteristic clinical features. After cardiac decompensation has lowered the blood pressure in hypertensive heart disease, chronic valvular disease, usually of acute rheumatic origin, may be simulated, but it may be excluded by the absence of history of rheumatic fever and by the absence of mitral and sometimes aortic contour.

V. PROGNOSIS

Prognosis depends in part upon the course of the essential hypertension. The more severe this is and the earlier it starts in life, the less favorable the outcome. The more rapid the development of arteriosclerosis and specifically coronary arteriosclerosis and its sequelae, the more severe the prognosis. Myocardial infarction and hypertension is less favorable than coronary occlusion and normal blood pressures.

Marked cardiac hypertrophy envisages increased overload, the development of ectopic rhythms and various degrees of heart block and coronary patterns suggest increasing cardiac disease. The occurrence of repeated attacks of angina emphasizes the development of coronary arteriosclerosis and insufficiency.

VI. GENERAL ASPECTS OF TREATMENT

Although hypertension and resultant hypertensive heart disease may often be expected to run their inexorable course, the intensity of the process, the rate of progression and the imponderable factors of heredity and environment are variable and therefore should emphasize therapeutic approaches.

The not uncommon experience that the internist has of observing some patients enjoying prolonged years of reasonably good health in the presence of marked arteriosclerosis should encourage the patient and stimulate the physician to anticipate preservation of health in measurable degree.

VII. TREATMENT

1. PREVENTIVE THERAPY

Any sound and effective therapy of arterial hypertension may be considered to be preventive treatment of hypertensive cardiac disease. Likewise the alleviation of such conditions as obesity, hyperthyroidism and diabetes mellitus should tend to lessen the ravages of hypertensive cardiac disease. The control of environmental factors, such as inordinate physical and nervous strain, may have significant benefits. Moderation in drinking, smoking and eating habits is highly desirable. Fats should be used sparingly. Adequate rest periods during the day and sleep at night should be sought. To secure relaxation in certain nervous individuals the use of sedatives

such as phenobarbital or of tranquilizing drugs may be necessary

2 ASYMPTOMATIC PERIOD

Granted that sinus rhythm is maintained when only cardiac hyperthrophy is apparent, conservative management as outlined above is adequate There may be difficulty in obtaining the patient's cooperation in the asymptomatic stage However, when diminished cardiac reserve is made apparent by dyspnea on exertion previously well tolerated, and when there is sometimes association with major disturbance of rhythm, the patient almost surely will seek relief and naturally cooperate in treatment Rest is of prime importance and if it is obtained in sufficient amount, that is, for many days and sometimes for weeks, alleviation of symptoms may occur with lessening of blood pressure and cardiac strain Digitalis may be of benefit at this stage but is not commonly used

3. PERIOD OF CARDIAC DECOMPENSATION

Failure of the left heart may occur suddenly or gradually and the course may be recurrent or chronic The discomfort of the patient with acute left heart failure, with paroxysmal nocturnal dyspnea, with cyanosis, cough and [illegible]

which follows prompt and adequate medical management The first step in such treatment is the use of morphine sulphate gr $^1/_4$ or gr $^1/_4$ or Demerol 50 mg or 75 mg followed by the use of O_2 by mask or tent, up to the point of adequate concentration The third step is prompt digitalization which, if the patient has not taken digitalis for $2^1/_2$ or 3 weeks, may be accomplished by one total dose or by the divided method If digitoxin is used and the total dose intended for digitalization is 1 2 mg to 1 8 mg intramuscularly, administration may be by one total dose More often in personal experience, one half of the total dose is given first, followed after a 6 to 8 hour interval by one fourth and by the remaining one fourth, if necessary for digitalization, after another 6 to 8 hour interval

Mercurial diuretics have won their place in treatment, Thiomerin or Mercuhydrin 1 to 2 cc is given intramuscularly at intervals to aid in transport of edema fluid, particularly that of the lungs Low sodium (500 mg) is also desirable to aid in such transport of edema A low calorie diet is advisable, with adequate protective elements As the right heart dilates and hypertrophies, venous engorgement of systemic veins, liver and splanchnic area occurs, sometimes with ascites and pleural effusion While myocardial irritability and auricular fibrillation may sometimes be alleviated by quinidine sulphate, digitalis is, by and large, the cardiac drug of choice when the effectiveness of the heart as a mechanical pump has become impaired

After restored compensation, the dosage of digitalis must be determined individually by finding the amount which will slow the ventricular rate to the 70s, and yet not precipitating intoxication with nausea, vomiting and sometimes ventricular tachycardia The maintenance dose of digitoxin is often 0 1 mg to 0 2 mg daily, more often the smaller dose or even less The patient's mode of life must be adjusted to his estimated myocardial reserve

It should be mentioned that not infrequently the pattern of heart failure is conditioned by the presence of coronary arteriosclerosis and later thrombosis which adds to the gravity of the cardiac status

CASE REPORT

Twenty-three years previously a 41 year old business man was first observed with the complaint of headaches His father had died of apoplexy at age 52 His mother, a hypertensive was living at age 71 One sister had hypertension and another was free from hypertension The outstanding initial finding was a blood pressure of 174/98 mm Hg When next re-examined 13 years later the blood pressure was 218/114 A blowing systolic apical murmur had appeared The two meter chest film showed transverse thoracic diameter of 31 1 cm and a transverse cardiac diameter of 15 9 with slight ventricular prominence "Tightness" through the substernal area produced by effort had appeared. Under symptomatic treatment, including nitroglycerin as nec-

essary health complaints were minimal and blood pressure varied from 172/108 to 234/110 Six years later angina had become more frequent During the last 5 years of life the patient suffered one attack of coronary thrombosis later an episode of acute left ventricular failure and still later partial right hemiplegia After the attack of acute failure there was a tendency for the hypertension to be lessened although the diastolic readings remained elevated though variable Death from acute cardiac failure ensued at age 64 Autopsy revealed marked coronary arteriosclerosis and myocardial fibrosis with marked left ventricular hypertrophy and cardiac weight of 630 gms

Shown in this case is (a) the hereditary influence in primary hypertension (b) onset before 50 years of age (c) persistently elevated although somewhat variable systolic blood pressure (d) the less variable diastolic blood pressure always sustained above 90 (e) the development of left ventricular hypertrophy, (f) the development of coronary sclerosis and insufficiency, (g) evidence of cerebral arteriosclerosis that led to partial hemiplegia and (h) death ensuing from acute left ventricular failure

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CHAPTER 30

Coronary Artery Disease: Some Aspects of the Natural History of Ischemic Heart Disease

WILLIAM BENNETT BEAN M D

"Every pain has its distinct and pregnant signification if we will but look for it"

—HILTON

DISEASE of the coronary arteries with its wake of decay and final ruin of myocardial function has been a fascinating study for physiologists pathologists clinicians electro cardiographers and others. For the people of an ageing society it has become the focal point of fear wonder and concern. Even the young men are not exempt. General textbooks of medicine and texts of cardiology contain excellent descriptions of varied clinical syndromes which attend coronary atherosclerosis. Whole volumes have been devoted to studies of the evolving changes in the electrocardiogram following myocardial infarction the less dramatic changes in the angina of acute coronary insufficiency induced by exercise or anoxia and the therapy of various symptoms which may result from an inadequate blood supply to the heart. There is less discussion of the relationship between the various clinical states which may prevail in the presence of coronary artery disease and a detailed consideration of the findings post mortem in patients who have died with myocardial infarction. Therefore this chapter will emphasize certain aspects of the disease which have received less attention. It cannot be comprehensive. Throughout this discussion certain arbitrary classes of disorders will be used for convenience but with an effort to keep in mind the fact that just as no two persons are alike no two hearts are identical. While we warp certain data into categories as a necessary method in analysis we are dealing with figments vital to our purpose but figments nonetheless. This is apparent to the wise physician immediately upon confronting the problems of a particular sick person. He must be governed by the phenomena of the patient not his own ideologies.

Coronary artery disease occupies several central positions in clinical medicine pathology physiology and human ecology. Its symptoms range from the absolute zero of what seems to be normal health to the overwhelming crisis of pain shock and death found in association with myocardial infarction. Disease in the coronary arteries may call attention to itself significantly in only three ways. These are pain in the chest disordered rhythm of the heart and congestive heart failure. Coronary artery disease may be silent clinically even though extensive pathologically. Its clinical fascination lies partly in the mystery of arteriosclerosis and partly in the very serious discrepancies we find when we try to relate symptoms to lesions. The problems may be illustrated by the unhappy error of interpretation made by Allbutt in the later years of a long life full of constructive medical wisdom. In his classic treatise on *Diseases of the Arteries Including Angina Pectoris* published in 1915 he came to grief in trying to fasten a symptom complex angina pectoris on a lesion aortitis. So elegant was his style and so imperious was his authority that a clearer understanding was held back for at least a generation. And he was guilty

of faults of logic against which he had inveighed *so effectively* in his earlier writings We still have too many examples of conviction *leading us* by the nose away from evidence

Pathologically, coronary arteriosclerosis can *be patchy or diffuse, localized to a single* point in one major vessel, or ramifying widely throughout all major vessels and their main branches Though roughly correlated with age, it can occur in newborn infants and be absent or mild in the very old Its incidence in the population rises, with increasing frequency as time goes on *The rate of the rise* and the percentage of persons affected in the United States today are both increasing This increase affects not only young men but even young women, for reasons we cannot explain Depending upon the anatomical design of the vessels, the degree of obstruction to the circulation, the presence and the extent of collateral circulation, the demands put on the heart, the arterial blood pressure, and no doubt many other factors severe disease of a coronary artery may *leave the myocardium structurally* and functionally nearly intact, or it may produce acute massive myocardial infarction or a diffuse muscle destroying fibrosis, or many miliary infarcts Ultimately there is apt to be ruin of a heart whose working capacity has been destroyed by the ischemic starvation which prevents an adequate flow of blood bringing oxygen fuel and building material and removing waste products through the various systems of venous drainage of the heart The most minute examination of *the* heart after death by injection plus dissection techniques and various other studies does not allow us to find lesions from which it can be said confidently in retrospect that the patient had little or much angina or congestive failure, or was relatively asymptomatic

Let us consider a hypothetical group of persons who have identical lesions in the coronary arteries advancing at identical rates of speed and progressing to the same ultimate outcome of *myocardial infarction When the* disease has become far enough advanced to produce angina in some of the group, and symptoms of breathlessness and perhaps a little ankle edema in others, there are many without symptoms If something else brings the patient to a physician no sign of heart trouble may be detected on a *scrupulously* careful study such as for an annual medical examination This situation is to be resolved only by recognizing wide bands of individual variability, the inadequacy of our *methods for* testing the integrity of the coronary blood supply during life, and the multifactorial nature of causality—what seems to be an identical symptom in many people may have many different causes and a single lesion may give rise to many different symptoms *What seems to be the same state of the coronary arteries,* in one person may give rise to severe pain, in another a mere twinge, in a third no symptom whatsoever, in a fourth some breathlessness with effort We may suppose that the threshhold for sensory perception varies widely for stimuli from the heart, as we know it does for measured painful stimuli in the skin It is possible, but has not been demonstrated, that those who are brought up short by pain may not be able to exercise to the point where they *experience breathlessness Likewise arterial* disease in the legs may halt activity before angina or breathlessness are provoked The person whose pain is less because fewer stimuli pass the threshhold, or whose physical reaction to pain is mild may strain his heart more as he can endure more activity These views are speculative but the discrepancy between the clinical patterns on the one hand and the physical state of the coronary arteries at autopsy on the other discloses one of our *important clinical puzzles*

In this chapter, I shall emphasize some of the clinical syndromes whose vaguely defined boundaries leave them now in one, now in another, clinical kingdom with shifting hegemony, owing allegiance first to one diagnostic group and then another and then another Occasionally a patient may fall properly into several groups Heart failure and angina may run hand in hand instead of as an either-or proposition Some emphasis will be placed upon the ecological aspects of myocardial infarction the clinical patterns, especially the atypical ones the sources of errors in diagnosis, and the complications, particularly *thromboembolism* and the not yet completely solved problems of treatment with anticoagu

lants In any clinical situation in which symptoms outrank signs as they do regularly in angina and often in myocardial infarction there can be no satisfactory experimental animals Man himself must provide us with all the information we can properly apply to his own problems This is vexing since we cannot marshall enough evidence to let logic give us the answer But this remains one of the charms of practical medicine and gives scope to the arts of the wise clinician

THE CORONARY ARTERIES

The gross architectural design of the coronary arteries and their general pattern has received detailed study by Schlesinger[43] using his injection plus dissection technique He found three different patterns of arterial distribution In group 1 with 48% of his specimens the right coronary artery predominates in the blood supply to the heart Reactions to arteriosclerosis in this group are intermediate between those of groups 2 and 3 Group 2 contained 34% of the specimens with the right and left coronary arteries supplying the heart in an even balance Hearts with this arrangement suffer the least effects from coronary arteriosclerosis In group 3 with 18% of the hearts the left coronary artery predominates in the blood supply to the heart These hearts suffer most from the effects of coronary arteriosclerosis The technique used permitted many hitherto unrecognized relations to be detected Some of the discordant relations of symptoms and lesions have been resolved by Schlesinger Blumgart and their associates Many remain It may be not so much the lining of the arteries and the quality of the fabric that determines subsequent cardiovascular difficulty but that a bad plan for the feed pipes for the pump was used in the blueprint It is a bad arrangement when the heart depends too much on the left coronary artery for its blood supply since when things go wrong the reserve system is not good and presumably the degree of collateral circulation coming in is not adequate

The appearance of anastomoses between macroscopic vessels of the coronary artery system has been a topic which has plagued investigations since Cohnheim s pronouncement that the coronary artery was an end artery This was given with great finality but it really just began the argument If the coronary artery is an end artery by definition there are no macroscopic anastomoses This belief was upset completely through the studies of Gross[2] who brought to the investigation of pathology imagination and valuable techniques He demonstrated (1) that anastomoses were found with increasing frequency with increasing age and (2) that the vasculature of the right ventricle did not increase with increasing age at the same rate as did that of the left ventricle so that it was relatively worse off than the left in older persons The general findings of Gross have been substantiated An entirely new interpretation was put on them by the classic studies of Schlesinger and Blumgart who demonstrated that indeed increasing collateral circulation was found with increasing age but this was not a result of mere aging A certain number of very old people had very adequate collaterals but the ischemia induced by coronary sclerosis and narrowing with or without actual coronary thromboses and not aging by itself called forth the collaterals They found that increased coronary artery anastomosis of older persons was a reflection of increased coronary artery disease This rather than some by product of aging itself they interpreted as the responsible mechanism The critical point which is not yet resolved is how quickly can collaterals grow in and how effective they will be in renewing the blood supply particularly when their own lumens are encroached upon by coronary sclerosis? Thus to what extent Herrick s "friendly neighboring arteries" can actually accomplish their mission of restoring the integrity of cardiac blood supply is determined by factors which we do not understand Certainly when a narrow artery by its best efforts is barely able to supply an area of myocardium with its basic needs for blood and

oxygen it sends out anastomoses to irrigate adjacent territory in the muscle only at the expense of its own primary responsibility

Older studies of the distribution of arterial disease and resulting myocardial damage suggested that *the anterior descending branch* of the left coronary artery be called "the artery of sudden death In many studies it has been *suggested* that *its thrombosis* or *its sclerosis* with subsequent infarction of the anterior wall of the left ventricle and portions of the interventricular septum constitute the commonest clinical form of myocardial infarction and that most frequently found at autopsy Studies with injection and dissection techniques bring some doubt about the primacy of the lesion but clinical experience and that in the autopsy room still reveal that anterior myocardial infarction is much more frequent *than other varieties and that the anterior des*cending branch of the left coronary artery is the seat of disease more commonly than are other coronary arteries or branches Its arteriosclerosis is likely to be more advanced

Geiringer in Scotland has made extensive studies of intimal vascularization and atherosclerosis in the coronary system with emphasis on the locus of the coronary artery What he calls the mural coronary for much of its length is enclosed within the muscle rather than being superficial and exposed on the epicardial surface He believes this protected position spares the vessel for he found that the mural *coronary escapes* atherosclerosis of the kind which is so common and so disastrous in vessels not thus exposed Geiringer s very convincing argument *has been called in question* by the observations of Edwards Burnsides Swarm and Lansing who failed to verify the freedom of intramural coronary *arteries from* arteriosclerosis Instead they found the extent and location of arteriosclerosis in the superficial and "mural" arteries to be erratic

Coronary arteriosclerosis may be the only arteriosclerosis In different vessels in any individual person it is quite variable in extent *severity and location* Whatever the general factors in its production there are local factors which are important We do not know what favors localization It may be concluded that *the stresses of torsion shearing and buckling* particularly at the right angle branching where the elements of the coronary artery break up and enter the myocardium may present forces which either damage the vessel wall or make it unduly susceptible to the development of atherosclerosis

The blood *supply to the artery wall itself* comes from two sources (1) the endothelium is bathed in the luminal blood flow and obtains *its oxygen and nutrients by direct diffusion* The remainder of the blood supply to the vessel wall itself comes by (2) the vasa vasorum from adventitial arteries and secondarily from intimal vascularization from new vessels which develop in association with the process of arteriosclerosis In healthy infants dying from accidents the intima is free from some disease in only a few This suggests that even at a very early age vascular trouble may have begun The area inside to the internal elastic lamella is avascular and only when it becomes approximately 0 35 mm thick in the coronary artery do intimal vessels grow in Observations by Dock suggest that intimal thickening in men is greater and begins earlier than in women This tendency for boys and men to have a thicker intima in the coronary vessels has been thought responsible for some of the sex differences in *incidence of angina and coronary artery* disease of various kinds

ARTERIOSCLEROSIS

Arteriosclerosis or atherosclerosis of the coronary arteries constitutes the one overwhelmingly important disease which slowly or abruptly starves or strangles the heart muscle and puts it out of commission Probing into the etiology and pathogenesis of sclerosis of *the coronary arteries* and arteriosclerosis is today the focal point of intensive research in many countries the world over A learned *society has as its sole purpose an* inquiry into arteriosclerosis The layman can scarcely read a few pages or a few paragraphs in his favorite

paper or journal without being assailed by someone's conviction and ideas quoted or misquoted They often revolutionize his dietary habits at least temporarily They may be contradicted with profound conviction next month or next year In spite of all the hue and cry most of the facts are still in the realm of natural history We do not have an adequate treatment and we have no cure for this increasingly prevalent disorder The closely held secrets of the finer aspects of intermediary metabolism lead again and again to cholesterol and fat but no one knows whether certain admitted correlations signify cause concomitance or effect Is disordered cholesterol metabolism prior to anything else the mechanism which finally ruins the artery or is this an early sequel or a mere concomitant? Does some primary force produce the earliest lesion in the arterial wall and a disordered cholesterol metabolism simultaneously Around these matters billow much heat and much smoke but little light has emerged One has the feeling that the fixed ideas the traditional beliefs the occluded mental fronts in the meteorology of opinion which determine the climate of contemporary thought are marking time for the emergence of new ideas and orientations which will set our thoughts on more fruitful lines of investigation

Cholesterol comes from dietary sources but in addition is manufactured by the body The structure of the cholesterol molecule is a basic one in many of the processes of life It is closely related for instance to the steroid hormones We know very little of the physical laws regulating the exchange of plasma lipids through the arterial endothelium It may be that intermittent or established hypercholesterolemia can coat the intima with waxlike material to a sufficient extent to interfere with the exchange of oxygen carbon dioxide and small carbon molecules which supply fuel Tiny ingrown stovepipes of wax may line the vessel wall and isolate it from its sources of supply Cholesterol may accumulate in subintimal and intimal cells through an intact membrane which indicates that there is a constant exchange of cholesterol in colloidal solution It seems to accumulate in the intimal cells only if the level of cholesterol in the blood is high for some time A classic example of one form of this is in familial xanthomatosis

The normal suspension of cholesterol in the blood stream a colloidal solution aggregated with protein usually preserved in its migration through the intact arterial intima may be upset somehow when it arrives in contact with the altered tissue substances of a diseased artery Ultimately this leads to precipitation of cholesterol in crystalline form Local concentration and other factors seem to determine the site and extent of such precipitation and the degree to which it is reversible Perhaps a disturbance of enzyme relations in the intimate metabolic economy of the tissue of the artery and its lining constitutes the earliest stage in what becomes morphologic arteriosclerosis Present day evidence suggests but does not prove that the increased frequency with aging represents the extension of the exposure in time rather than a process intrinsic in the wear and tear of aging itself The final crux of the matter of whether the vessel wall itself is diseased first and the changes occur from imbibition or infiltration of cholesterol from the plasma or whether there is a primary disorder in lipid metabolism which can affect and disorganize a structurally normal vessel We do not know Did cholesterol damage the vessel or did it come in only after damage was done because as the explorers said about climbing Everest—"It was there"

In sequence the first lesions consist of a plaque of fairly loose connective tissue with young fibroblasts deposits of amorphous material with few cholesterol crystals freedom from calcium absence of vascularization from the media early deterioration of the internal elastic lamella and minimal fibrosis of the media In the next stage the plaque has more extensive deposits of cholesterol Its base is hyalinized Scarring is beginning with a condensation of the fibrous material containing few fibroblasts Early vascularization from the media is appearing and there may be small calcium deposits physical disruption of the tissue apparently from cholesterol scarring and loss of substance in the media with some vascularization and further deterioration of the internal elastic lamella When the process is advanced calcium is deposited in large ag

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Geringer in Scotland has made extensive studies of intimal vascularization and atherosclerosis in the coronary system with emphasis on the locus of the coronary artery. What he calls the mural coronary for much of its length is enclosed within the muscle rather than being superficial and exposed on the epicardial surface. He believes this protected position spares the vessel for he found that the mural coronary escapes atherosclerosis of the kind which is so common and so disastrous in vessels not thus exposed. Geringer's very convincing argument has been called in question by the observations of Edwards, Burnsides, Swarm and Lansing who failed to verify the freedom of intramural coronary arteries from arteriosclerosis. Instead they found the extent and location of arteriosclerosis in the superficial and "mural" arteries to be erratic.

Coronary arteriosclerosis may be the [illegible] arteriosclerosis. In different vessels in an individual person it is quite variable in extent, severity and location. Whatever the general factors in its production there are local factors which are important. We do not know what favors localization. It may be concluded that the stresses of torsion, shearing and buckling, particularly at the right angle branching where the elements of the coronary artery break up and enter the myocardium, may present forces which either damage the vessel wall or make it unduly susceptible to the development of atherosclerosis.

The blood supply to the artery wall itself comes from two sources: (1) the endothelium is bathed in the luminal blood flow and obtains its oxygen and nutrients by direct diffusion. The remainder of the blood supply to the vessel wall itself comes by (2) the vasa vasorum from adventitial arteries and secondarily from intimal vascularization from new vessels which develop in association with the process of arteriosclerosis. In healthy infants dying from accidents the intima is free from some disease in only a few. This suggests that even at a very early age vascular trouble may have begun. The area inside to the internal elastic lamella is avascular and only when it becomes approximately 0.35 mm thick in the coronary artery do intimal vessels grow in. Observations by Dock suggest that intimal thickening in men is greater and begins earlier than in women. This tendency for boys and men to have a thicker intima in the coronary vessels has been thought responsible for some of the sex differences in incidence of angina and coronary artery disease of various kinds.

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paper or journal without being assailed by someone's conviction and ideas quoted or misquoted They often revolutionize his dietary habits at least temporarily They may be contradicted with profound conviction next month or next year In spite of all the hue and cry, most of the facts are still in the realm of natural history We do not have an adequate treatment and we have no cure for this increasingly prevalent disorder The closely held secrets of the finer aspects of intermediary metabolism lead again and again to cholesterol and fat but no one knows whether certain admitted correlations signify cause concomitance or effect Is disordered cholesterol metabolism prior to anything else the mechanism which finally ruins the artery or is this an early sequel or a mere concomitant? Does some primary force produce the earliest lesion in the arterial wall and a disordered cholesterol metabolism simultaneously Around these matters billow much heat and much smoke but little light has emerged One has the feeling that the fixed ideas the traditional beliefs the occluded mental fronts in the meteorology of opinion which determine the climate of contemporary thought are marking time for the emergence of new ideas and orientations which will set our thoughts on more fruitful lines of investigat on

Cholesterol comes from dietary sources but in addition is manufactured by the body The structure of the cholesterol molecule is a basic one in many of the processes of life It is closely related for instance to the steroid hormones We know very little of the physical laws regulating the exchange of plasma lipids through the arterial endothelium It may be that intermittent or established hypercholesterolemia can coat the intima with waxlike material to a sufficient extent to interfere with the exchange of oxygen carbon dioxide and small carbon molecules which supply fuel Tiny ingrown stovepipes of wax may line the vessel wall and isolate it from its sources of supply Cholesterol may accumulate in subintimal and intimal cells through an intact membrane which indicates that there is a constant exchange of cholesterol in colloidal solution It seems to accumulate in the intimal cells only if the level of cholesterol in the blood is high for some time A classic example of one form of this is in familial xanthomatosis

The normal suspension of cholesterol in the blood stream a colloidal solution aggregated with protein usually preserved in its migration through the intact arterial intima may be upset somehow when it arrives in contact with the altered tissue substances of a diseased artery Ultimately this leads to precipitation of cholesterol in crystalline form Local concentration and other factors seem to determine the site and extent of such precipitation and the degree to which it is reversible Perhaps a disturbance of enzyme relations in the intimate metabolic economy of the tissue of the artery and its lining constitutes the earliest stage in what becomes morphologic arteriosclerosis Present day evidence suggests but does not prove that the increased frequency with aging represents the extension of the exposure in time rather than a process intrinsic in the wear and tear of aging itself The final crux of the matter of whether the vessel wall itself is diseased first and the changes occur from imbibition or infiltration of cholesterol from the plasma or whether there is a primary disorder in lipid metabolism which can affect and disorganize a structurally normal vessel We do not know Did cholesterol damage the vessel or did it come in only after damage was done because as the explorers said about climbing Everest—"It was there

In sequence the first lesions consist of a plaque of fairly loose connective tissue with young fibroblasts deposits of amorphous material with few cholesterol crystals freedom from calcium absence of vascularization from the media early deterioration of the internal elastic lamella and minimal fibrosis of the media In the next stage the plaque has more extensive deposits of cholesterol Its base is hyalinized Scarring is beginning with a condensation of the fibrous material containing few fibroblasts Early vascularization from the media is appearing and there may be small calcium deposits physical disruption of the tissue apparently from cholesterol scarring and loss of substance in the media with some vascularization and further deterioration of the internal elastic lamella When the process is advanced calcium is deposited in large ag

oxygen, it sends out anastomoses to irrigate adjacent territory in the muscle only at the expense of its own primary responsibility

Older studies of the distribution of arterial disease and resulting myocardial damage suggested that the anterior descending branch of the left coronary artery be called "the artery of sudden death" In many studies it has been suggested that its thrombosis or its sclerosis with subsequent infarction of the anterior wall of the left ventricle and portions of the interventricular septum constitute the commonest clinical form of myocardial infarction and that most frequently found at autopsy Studies with injection and dissection techniques bring some doubt about the primacy of the lesion but clinical experience and that in the autopsy room still reveal that anterior myocardial infarction is much more frequent than other varieties and that the anterior descending branch of the left coronary artery is the seat of disease more commonly than are other coronary arteries or branches Its arteriosclerosis is likely to be more advanced

Geiringer, in Scotland has made extensive studies of intimal vascularization and atherosclerosis in the coronary system with emphasis on the locus of the coronary artery What he calls the mural coronary for much of its length is enclosed within the muscle rather than being superficial and exposed on the epicardial surface He believes this protected position spares the vessel for he found that the mural coronary escapes atherosclerosis of the kind which is so common and so disastrous in vessels not thus exposed Geiringer's very convincing argument has been called in question by the observations of Edwards, Burnsides, Swarm and Lansing, who failed to verify the freedom of intramural coronary arteries from arteriosclerosis Instead they found the extent and location of arteriosclerosis in the superficial and "mural" arteries to be erratic

Coronary arteriosclerosis may be the only arteriosclerosis In different vessels in any individual person it is quite variable in extent severity and location Whatever the general factors in its production there are local factors which are important We do not know what favors localization It may be concluded that the stresses of torsion, shearing and buckling particularly at the right angle branching where the elements of the coronary artery break up and enter the myocardium, may present forces which either damage the vessel wall or make it unduly susceptible to the development of atherosclerosis

The blood supply to the artery wall itself comes from two sources (1) the endothelium is bathed in the luminal blood flow and obtains its oxygen and nutrients by direct diffusion The remainder of the blood supply to the vessel wall itself comes by (2) the vasa vasorum from adventitial arteries, and secondarily from intimal vascularization from new vessels which develop in association with the process of arteriosclerosis In healthy infants dying from accidents the intima is free from some disease in only a few This suggests that even at a very early age vascular trouble may have begun The area inside to the internal elastic lamella is avascular and only when it becomes approximately 0 35 mm thick in the coronary artery do intimal vessels grow in Observations by Dock suggest that intimal thickening in men is greater and begins earlier than in women This tendency for boys and men to have a thicker intima in the coronary vessels has been thought responsible for some of the sex differences in incidence of angina and coronary artery disease of various kinds

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gregates, broad vascular channels go into the perimeter of the plaque from the adventitia by way of the media, advanced hyalinization occurs and *fibroblastic activity is at a minimum* The internal elastic lamella may be badly damaged or almost completely destroyed There is now advanced fibrosis of the media Ultimately there may be a dissecting hematoma or ulceration of the intima with thrombus formation So much then for the *microscopic* evidence Among the contributing factors are increasing age, male sex, hypertension, diabetes, familial tendency to high serum cholesterol as in xanthomatosis, hereditary tendency, obesity and muscular or mesomorphic body type No doubt there are other factors of race, inheritance, geographic location, occupation, and the like The rarity of coronary artery disease of a clinically significant type in women of the childbearing age has recently been called to question but in my experience this is still an outstanding clinical fact

CLINICAL COURSE

To what extent clinically important artery disease is reversible is unknown We cannot obtain in vivo a clear picture of the location or extent of coronary artery disease Angiographic techniques seem unlikely to resolve this problem for the present In infants, children, and young adults, one commonly finds cholesterol plaques in the coronary arteries of those who have died of unrelated causes There is some statistical evidence to suggest that plaques which occur in children and adolescents may disappear and in later adult life either a new process or a return of the old process develops under the influence of a multitude of factors Coronary artery disease localized as it is in an unpredictable fashion reduces the resilience and reactivity of the *coronary artery tree, diminishes the basal or* maximal blood flow, gives rise to severe sclerosis, intimal ulcers, small dissecting hemorrhages leading to hematomas, and subsequently thrombosis of the lumen Depending upon the rate of advance of this process, the heart may make certain adjustments by calling in collateral circulation which may ready the heart of a person with slowly developing arterial disease for subsequent acute damage This preparation is not available to one whose disease develops quickly or in whom a thrombus plays its part early in occluding the lumen

CORONARY VENOUS THROMBOSIS

It has always worried me that the coronary veins have been studied only in the most cursory manner at autopsy examinations and I have speculated about whether thromboses in the coronary vein system might not give rise to hemorrhagic infarction of the heart[6] An occasional case of phlebitis of the coronary veins has been recorded but these are thought of so rarely as to be true medical oddities It would be of much interest to see whether systematic examination of the veins revealed thromboses more often in those examples of acute myocardial infarction where no thrombus exists in the arteries and the degree of arteriosclerosis is not extreme

PAIN IN THE CHEST

GENERAL REMARKS—SOME QUOTATIONS FROM LATHAM

"It would be a great thing to understand Pain in all its meanings"

"The first thing to be noticed is the difficulty we have in judging of Pain as a symptom which we do not find in respect of other symptoms"

"No man wise or foolish, ever suffered Pain who did not invest it with a quasi materialism"

'I have known many a philosopher, outreasoned by his feelings, take to rating and chid-

ing his Pain, as if it were an entity or quiddity of itself"

"Admitting our patient honest and his Pain real, how are we to make sure of its degree?"

"In matters of feeling we must depend entirely upon what our patient tells us Every man smarts with his own pain, himself, and nobody else, can say how much"

"Not only degree of pain, but its existence in any degree, must be taken upon the testimony of the patient"

"Whatever sick bed we stand by, and hear severe Pain complained of, and find it the accompaniment of febrile or sudden or rapidly progressive disease, we must not leave that bedside until we have satisfied ourselves whether anything, or what, is to be done expressly for the Pain"

"Pain may kill It may overwhelm the nervous system by its mere magnitude and duration"

"The sense of Pain is in proportion to the magnitude of the disease only within certain limits The extremity of the disease may abate or even abolish the sense of Pain altogether"

"Pain, itself a thing of life, can only be tested by its effects upon life, and the functions of life And whether it be small or great (so to speak), or of whatever degree, it is to its effect upon life and the function of life that we must look, if we would know the part it acts pathologically, and what it requires remedially in individual cases"

TOWARD AN ANALYSIS OF PAIN

Coronary artery disease cannot be discussed without emphasis on the whole problem of pain and our present doctrines about it It is around the phenomenon of pain that are centered our mistakes in interpreting it when present and being misled by its absence Its central position with respect to ischemic heart disease is ample justification for a review of pain and a judgment of its several specific elements

For a person to experience pain, we require (1) a stimulus, next (2) a mechanism for transmission of an impulse or nerve passage to (3) the area where perception seems to occur, namely in the higher levels of the central nervous system, although precisely where and how we do not know Next, in order to get any understanding of pain in a person other than ourselves we must rely on two further responses to pain The first is (4) the patient's description of it which depends upon his intelligence imagination, clarity of mental processes at the time, his prior experience with pain and innumerable other factors The other is (5) his response or reaction to pain which may give us additional and sometimes objective information Patterned or disorganized physical responses to pain may be reflex, or unconscious, or they may be voluntary Thus a person who barks his shin withdraws from the stimulating object with a prompt and involuntary reaction Then a patterned voluntary response follows with rubbing the shin, looking at it, and making such comments as seem appropriate for the occasion

In my own efforts to analyze pain and its manifestations and in the determination of its significance, I find it convenient to use the following plan in detective work Many other methods are equally valuable The main thing is to have some system which we pursue as a fixed and obligatory routine so that we do not overlook any important aspects or pain

LOCATION

The first thing we need to know about pain is where it is and there are three points that I inquire after, all in a cluster They refer to the geography, that is, (1) the *situation*, the (2) *localization*, and the paths of (3) *extension* or *reference* By situation we mean whether the pain is on the surface, in the skin, goes deep, or exists only deep Localization tells us whether the painful area can be covered with a point of a pencil, a finger, or the hand, or is still more diffuse, whether the area is constricted or extended one By these inquiries we get a notion of pain in three di

mensions so that we can visualize it as having a locus in a solid body This is a useful fiction The third point includes extension of pain by the invasion of contiguous territory as for instance along a nerve where pain is perceived as a continuum rather than a simultaneous but different pain at two separate and distinct places By referral is meant pain perceived as at a distant site without continuity between it and what we conceive as the primary locus

CHARACTERISTICS

The next features I inquire about are even less tangible They include descriptions of (4) the *character* and (5) the *severity* of the pain The best we can make out of the character of pain is some analogy to a familiar traumatic situation The patient says that the pain is burning crushing stinging throbbing cramp like or uses some other simile The information we get from this line of inquiry is proportional to our past experience and the imagination and descriptive ability of the patient Even in uneducated people this information may be very vivid and very exact but it tends to be rather diffuse In estimating severity it is important insofar as we are able to distinguish between the complaint volunteered insistently by overresponsive persons who exaggerate every minor symptom into a major disaster and those stoical persons who minimize even very serious disturbances Having learned about pain in terms of kind and degree we pursue the inquiry into the field of chronology

CHRONOLOGY

The third *group of facts* regarding pain concerns the *temporal diurnal and calendar time relationships* Number (6) in this group is *duration* Is the pain a flash of lightning which appears for an instant and is gone is it one of slow but steadily rising intensity which builds up to a peak and then slowly fades out or does it establish itself at an agonizing plateau of anguish and misery? Is it a constant pain which endures for many hours or a brief pain which is a nuisance rather than a crisis? The next factor is (7) the *frequency* of pain *by which we attempt to get the chronology* and the calendar pattern Is the pain *habitual and inveterate? Does it come every day or many* times a day or only on sporadic and unforeseen occasions Is it an irregular or recurring episode? *Has it happened only once?* Since we know that many pains follow fairly characteristic patterns we may obtain useful information from this inquiry

In the next category are included (8) the *special times* or circumstances when pain occurs They include those *acts situations or* events which occur regularly as antecedants or *concomitants of pain For instance* does a given degree of exercise *invariably induce it?* Does it have a relationship to meals? Is it provoked by motion or only by emotion? Does it seem to result from the *reactions of* the body to the trials and turmoil of everyday life or any particular and peculiar emotionally charged circumstance? Is there a seasonal or weather relationship? Important clues may lie in the answers to such questions

INDUCED INFLUENCES

The other categories relate to the situations which persons suffering from pain have found (9) to *aggravate* or (10) to *relieve* the pain to induce it or to end it Much information can be obtained from careful evaluation of these features One should separate if possible those stimuli which simply make an existing pain worse and those circumstances which seem to induce the pain de novo In other words when the pain is there what makes it *worse? If there is no pain what makes it* come on? Is it made worse by activity movement heat cold driving a car excitement exercise or whatnot? Do certain foods produce it or does any kind of large meal produce it? Will eating stop it? Will an abrupt halt to activity relieve the pain? Is there a position of ease or a posture in which pain is provoked alleviated or eliminated? Have special procedures or medicines been effective? Are there any regular signs or symptoms which attend it—dyspnea rigors faintness angor animi eructation or passage of flatus abdominal rumblings borborygmus *flushing or something* else?

TOPOGRAPHICAL ANATOMY OF PAIN IN THE CHEST

While the patient's story gives us our first and most important clues about pain it must be analyzed in the examination of the patient This constitutes the next step in the progression from an analysis to synthesis of the clinical problem This stage of the analysis has for its purpose obtaining an answer to one question—What structures are found in or near or related to the site or sites where pain is felt?

Protecting and supporting structures The highly sensitive skin of the body has sensory nerves of a high degree of specificity and acute sensibility Much referred pain is interpreted by the brain as coming from the acutely sensitive structures innervated from the same segment as a disturbed viscus which gives rise to the primary stimuli A skeleton with joints with periosteum bones tendons ligaments must be considered in the examination of the patient for evaluating pain

Muscles The degree of participation of striated muscle in referred pain by induced spasm has never been logically settled although there is some evidence that it is important As an example of the role of visceral organs in inducing pain the spasm of smooth muscle the colicky contraction of the alimentary canal or the ureter give good examples and abdominal rigidity in itself may produce a pain clearly enough as may the tetanic contractions of tetanus or tetany

We must consider the *peripheral nerves* themselves and in addition the sounding board of the central nervous system These must be remembered as potential sites for a lesion or process which induces pain interpreted as coming at a distance from the true location of the difficulty Herpes zoster is an example

The *diaphragm* may give rise to pain interpreted as coming from the heart It ranges anywhere from a stitch in the side which occurs on running to the pain of subphrenic abscess or diaphragmatic pleuritis or pericarditis

The *alimentary canal* with lesions and functional disorders of the esophagus includes diverticula twitches and spasm hiatus hernia peptic ulcer pancreatitis gall bladder disease and painful ischemia of mesenteric vessels (abdominal angina)

Mediastinal structures and disorders induced in them by such things as inadequate blood supply metastatic tumors and inflammatory reactions enlarged lymph nodes and "collagen disease"

The *lungs and pleura* particularly with reference to pulmonary infarction pneumothorax pleurisy pneumonia tumors

The *great vessels* with emphasis on hemorrhagic dissection and various forms of aneurysm

Miscellaneous general states such as anemia thyrotoxicosis and polycythemia

And last but most important the *heart* itself to which this chapter is mainly devoted

CORONARY ARTERY DISEASE

ANGINA PECTORIS

The symptom complex of angina pectoris has had the earnest attention of physicians and patients probably long before Heberden wrote his beautiful description of the symptom complex and provided its *dramatic name* *It has* been a favorite battle ground in the inky warfare of medical polemics a stimulus to the imagination and fickle fancy of the systematists and the happy hunting ground for the theorists—witness Huchard's collection of 80 different theories about its pathogenesis some 60 years ago Although in major outlines we understand its pathogenesis its intimate association with structural disease of the coronary arteries its pathophysiology of pain induced by muscle ischemia there is sufficient variability from patient to patient that differential diagnosis tests the skill of the finest clinician It merges at the one extreme into neurosis and at the other it develops into or eventuates in myocardial infarction or heart failure Perhaps there is no better introduction to this subject than to quote from Heberden's original account

TABLE I

The following is a list of personally encountered conditions in which a diagnosis of angina or myocardial infarction finally *turned out to be*

I *Diseases of the Heart and Aorta*

1 Pericarditis
2 Dissecting aneurysm
3 Rupture of aortic cusp
4 Arteriosclerotic aneurysm
5 Syphilitic aortic aneurysm
6 Aortic regurgitation
7 Coronary osteal stenosis
8 Aortic stenosis
9 Massive embolus to the heart
10 Ball valve thrombus
11 Acute cor pulmonale
12 Metastatic tumor of the heart
13 Primary tumor of the heart
14 Acute rheumatic fever
15 Cardiac tamponade from indirect injury
16 Paroxysmal arrhythmias
17 Coronary arteritis
18 Pericardial infarct
19 Scleroderma heart
20 Polyarteritis of the coronary arteries

II *Lungs and Pleura*

1 Pulmonary embolus
2 Pulmonary infarction
3 Pneumothorax with or without tension
4 Interstitial pulmonary emphysema
5 Pleurisy
6 Pleural effusion
7 Pneumonia
8 Pleural adhesions
9 Bronchiectasis
10 Lung abscess
11 Bronchogenic carcinoma
12 Metastatic carcinoma
13 Epidemic pleurodynia
14 Rib fracture
15 Trauma without recognizable injury to the heart

III *Esophagus and Diaphragm*

1 Cardiospasm
2 Esophagitis with peptic ulcer of the esophagus
3 Carcinoma
4 Rupture of the esophagus
5 Peptic ulceration of the esophagus
6 Peptic ulceration of the stomach
7 Ruptured peptic ulcer
8 Esophageal diverticulum
9 Esophageal hiatus hernia
10 Diaphragmatic flutter
11 Diaphragmatic pleurisy
12 Subdiaphragmatic abscess

IV *Chest Wall and Mediastinum*

1 Muscle strain and trauma
2 Fibrositis
3 Bursitis
4 Myalgia
5 Neuralgia with trigger point pain
6 Mastitis
7 Gynecomastia
8 Costochondritis of the costosternal junction
9 Mediastinitis
10 Mediastinal tumor
11 Shoulder girdle lesions
12 Acute thyroiditis
13 Acute hemorrhage into the thyroid

V *Central Nervous System*

1 Intercostal neuritis
2 Pleurodynia
3 Herpes zoster
4 Neurofibromatosis
5 Tabes dorsalis
6 Extradural cord tumor
7 Metastatic cord tumor
8 Epidural abscess
9 Cervical arthritis
10 Cervical disc
11 Spinal caries
12 Spondylitis deformans
13 Radiculitis
14 Brachial neuritis
15 *Neurovascular syndromes*
16 Hand shoulder syndrome

VI *Abdomen*

1 Gall stone colic
2 *Acute cholecystitis*
3 Carcinoma of the gall bladder
4 Peptic ulcer of the stomach
5 Peptic ulcer of the duodenum
6 Ruptured peptic ulcer
7 Dumping syndrome
8 Intrinsic abscess of the liver
9 Subphrenic abscess
10 Acute congestion of the liver with right ventricular failure
11 Peritonitis
12 Pancreatitis
13 Infarct of the mesentery
14 Infarct of the kidneys
15 Infarct of the spleen
16 Appendicitis
17 Splenic flexure syndrome

VII Miscellaneous

1 Severe anemia
2 Insulin reaction
3 Spontaneous hypoglycemia
4 Effort syndrome
5 Cardiac neurosis
6 Diabetic coma
7 Myxedema after withdrawal of therapy
8 Myxedema with too rapid thyroid application
9 Morphine withdrawal
10 Narcotic addiction
11 Glomus tumor
12 Malingering
13 Thyroid crisis in Grave's disease
14 Pheochromocytoma
15 Gower's syndrome
16 Angina vasomotoria
17 Diencephalic syndrome
18 Paroxysmal pain associated with cerebral dysrhythmias
19 Syndrome of metastatic carcinoid
20 Anaphylactic reaction
21 Injection of pitressin
22 Injection of priscoline
23 Acute porphyria

"There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called Angina pectoris
Those, who are afflicted with it, are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away, if it were to increase or to continue the moment they stand still, all this uneasiness vanishes In all other respects, the patients are at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different
After it has continued some months, it will not cease so instantaneously upon standing still, and it will come on, not only when the persons are walking, but when they are lying down When a fit of this sort comes on by walking, its duration is very short, as it goes off almost immediately upon stopping
When I first took notice of this distemper, and could find no satisfaction from books, I consulted an able physician of long experience, who told me that he had known several ill of it and that all of them had died suddenly This observation I have reason to think is generally true of such patients, having known six of those, for whom I had been consulted die in this manner, . The os sterni is usually pointed to as the seat of this malady, but it seems sometimes as if it was under the lower part of it, and at other times under the middle or upper part, but always inclining more to the left side, and sometimes there is joined with it a pain about the middle of the left arm What the particular mischief is, which is referred to these different parts of the sternum, it is not easy to guess, and I have had no opportunity of knowing with certainty .
Time and attention will undoubtedly discover more helps against this tiezing and dangerous ailment "

The patient with angina has a symptom complex in which pain is the predominant feature Let us analyze the pain according to the ten modalities discussed previously (1) *Situation* The pain is in the front part of the chest, often midline, under the middle or upper portion of the breastbone, tending at times to be felt more on the left than on the right (2) *Localization* It may cover an area encompassed by the palm or by both hands, though occasionally it seems to be much smaller (3) *Extension* It may extend deep, occasionally be felt well within the chest, though not very often going through to the back It may irradiate up into the base of the neck, the jaw, the shoulders, down the arm, particularly the medial aspects or it may be *referred* to these areas in varying combinations Sometimes paresthesia with numbness and tingling, better describes a sensation in the arms and hands (4) *Quality* The pain is likely to be described as constricting, choking, squeezing, pressing, strangling as though there was a weight on the chest or some tremendous external pressure Matthew Arnold described the sensation as

"the peak of a mountain pressing in on the chest. This sense of pressure and constriction was explained by Mackenzie as resulting from actual intercostal muscle spasm. I believe there is some analogy with the symptoms which occur when one 'has his wind knocked out.'" (5) *Severity.* The pain of angina is a severe pain. It is a rare patient who is able to continue activity in the face of it, though on occasion one may walk it off. The victim is stopped in his tracks, brought up short, and must wait until a few moments have passed or nitroglycerin has brought relief. (6) *Duration.* The attack occurs out of the blue with little or no warning. Pain beginning abruptly, *waxing in intensity for a few seconds up to a* minute or so, rarely lasting longer than ten minutes. Most patients tend to exaggerate the actual duration of an attack. If measured by a watch, attacks range between 2 and 5 minutes, rarely exceeding 10 minutes. If an attack lasts longer than 15 minutes, one should suspect something other than simple angina. (7) The *frequency* of attacks depends to some extent on the severity of the disease. They are separated widely when the symptoms begin and later come more and more frequently. There is much variability depending upon the number of unavoidable stimuli to which the patient is exposed. One of the characteristics is that it is regularly brought on by (8, 9) a *specific degree* of activity under *regular* circumstances, such as in walking up a hill towards work. The same work load of another variety will evoke it. It is characteristic for angina to come on during the exercise but only after a certain amount of exercise has occurred. It is not like muscular or arthritic pains which are induced by motion, nor is it like some examples of pain with aortic stenosis which may come on after the exercise is over. It intermits through the seasons and through the years, more prevalent in cold weather and tending to increase in frequency as the underlying coronary disease *progresses. It is more* common after meals, may be provoked by excitement and emotion. John Hunter spoke feelingly of his angina and his trouble at hospital board meetings by saying "my life is in the hands of any rascal who chooses to annoy and tease me." Some of the provoking circumstances are additive so that any combination of exercise, a large meal, emotion or cold weather increase the probability of an attack in the victim of angina. Of the influences which *aggravate* or *relieve* the pain, *most patients find quickly that activity brings it on and sudden cessation of activity tends to halt it.* (10) The *relief* of the pain by *stopping activity or by the use of nitroglycerin is* characteristic.

Angor animi, the organic sensation of impending dissolution, a sensation which I suppose can be understood only by those who have felt it, has been described in elaborate and meticulous detail by John Ryle, who was *himself a victim of the most extravagant variety of this distressing symptom.* It should be differentiated from the conviction that death *is imminent. This might be the reckoning of* a perceptive physician with angina. It is not the passionate desire for death which may occur in a severe attack, which usually is reserved for persons suffering extreme anguish with myocardial infarction or dissecting aneurysm. Angor animi is well worth searching for in persons with chest pain because although it seems to be mediated by some disorder of function or structure of the medulla, it goes hand in glove with angina pectoris. Numerous other symptoms such as dyspnea, faintness, abdominal rumblings, flushings and *syncopal attacks may occur severally or may* all be absent. It is rare for any patient to *experience more than one or two of such con*comitants with a given attack. Furthermore there is a tendency for each patient to have fairly similar attacks.

One of the remarkable things about persons subject to angina is the complete sense of well being which is likely to prevail after the attack has gone by. It almost defies the credulity of the victim that he can be so desperately uncomfortable at one moment and so comfortable a little while later.

Prinzmetal has recently described what he believes to be an important subvariety of angina characterized by pain coming on at rest, sharp waxing and waning with a pain which occurs in waves and characteristic electrocardiographic changes which may foretell the sight of a future myocardial infarct.

INFARCTION OF THE HEART

Myocardial infarction is a stage in the evolution of coronary arteriosclerosis often but not invariably resulting from thrombosis of one or more coronary arteries

THE BACKGROUND

In any large population group in our Western culture certain elements are more likely to have coronary disease than others Men suffer more and are affected at a younger age than women though there is a suggestion that even this sex difference is diminishing Certain genetic strains not as yet clearly defined are prone to develop vascular disease Diabetes hypertension obesity a body build heavy and thick each adds to the risk Rheumatic fever and syphilis are of little importance In the main we cannot influence the quality of our vascular tubing and some is poor with a tendency to wear out early and some is good What hope we have for prevention lies in proximate causes about which are now seething ideas and speculation which have far outrun our modicum of hard won facts

THE FOREGROUND

Arteriosclerosis of the coronary arteries leading to confining strictures of the arterial network hematomas which rumple and obstruct the lumen intimal disease with thrombosis which encroaches on or obstructs the channel these are the central culprits Cholesterol is the villain but how and why and even how much we do not know The best efforts of our wisest scientists to measure cholesterol s importance have wound up in a stalemate [1] Even this would have been more convincing if the interpretations had not coincided so neatly with the existing schools of belief

We see a wave of enthusiastic but usually temporary dieting by a populace bewildered by the oscillating pundits who advise pro and con fats unsaturated fats cholesterol calorie restriction desalting vegetable sterols violent exercise and whatnot The average physician acting as indeed he is in this arena a bemused layman often forgets the years and indeed decades of painstaking research with almost impossibly elaborate controls needed to solve even a little the knotty problems of a chronic process such as arteriosclerosis This much seems sure that a calorie intake balanced with expenditure careful regulation of diabetes careful reduction of high blood pressure moderation in the use of tobacco and alcohol and a life where strain is faced and met when not avoidable are all we can suggest to our worried patients Few physicians can hold themselves up as models for what they urge by precept

If we knew the exact circumstances which favor the actual formation of a thrombus in a coronary artery we might proffer a tardy prophylaxis We do not have nor is it likely that we will soon have methods for exact measurement of patency reactivity and the intimate hemodynamic affairs of the coronary circulation during life Some help comes from experimental animals but there is no near counterpart of man with a spontaneous disease The best clues we can get come from comparing what is found at death with a well kept record of the natural history of the patient A few facts have emerged from studies of such problems If the actual beginning of coronary thrombosis or myocardial infarction is reflected in the onset of pain or sometimes acute heart failure no time of day or night neither work nor play nor rest is safe Though no man can rightly serve as his own control violent exertion adds some risk and should be avoided Hemorrhage shock, occasionally major surgical operations or trivial procedures such as thoracentesis may initiate the pain Profound hypoglycemia alcoholic intoxication overuse of nitroglycerin and acute infections probably have some hazard and to this list may be added severe trauma The cold winter months and the changeable spring season contain some added danger at least in some regions but how such seasonal tides work their hurt is unknown In short the person who harbors significant coronary artery disease whether with angina or other

signal or silent is living under the sign and omen of trouble manifest or hidden He should live the life of a philosopher avoiding excesses living with repose of spirit with the proper hygienic regard for his body and the right employment for the mind But who of *us does?*

Sometimes a person with a consistent pattern of anginal attacks will notice a change in the quality of pain or angina will begin mildly and modestly de novo Such a *prodrome* may be the harbinger of an impending catastrophe It calls for prompt treatment with anticoagulants Unhappily most prodromes are recognized only in retrospect after a major attack and even prompt prophylaxis may not prevent disaster Such symptoms in preview may occur with infarction without fresh thrombosis though usually they are assumed to mean a developing thrombus

THE TYPICAL ATTACK

The usual attack of myocardial infarction stands as the best delineated clinical picture of our age and serious errors in diagnosis result from too confident ascription of chest pain to infarction and failure to think of the masquerades or an awareness of silent infarctions

The dramatic urgency of a serious attack is indeed spectacular Out of a past free from serious complaint or as part of the evolving pattern of angina pectoris with or without prodromes pain seizes the body mind and whole being of the patient This is no ephemeral anguish but an overpowering agony compact of a sense of crushing strangling squeezing to which is added some trouble with breathing which may pass nearly unnoticed in the more urgent sense of pain The pain is retrosternal epigastric tending a little more to the left than the right and often irradiating or being referred into the shoulders the neck the lower jaw and throat and down both arms or only the left side Added to the pain in areas of reference or replacing it is the numbness and tingling of a paresthesia Dyspnea the most common symptom usually is not troublesome at first but may go on to orthopnea or Cheyne Stokes respiration Cough is common and there may be engorgement of the neck veins cyanosis and sweating as the elements of clinical shock gain the ascendency Vomiting is common even before morphine is used and morphine may induce or increase nausea and vomiting Restlessness thrashing about even mania and suicide may occur The sense of imminent death the all pervading sensation of being in the process of death—angor animi is common though rarely does a patient describe it voluntarily It is not the rational belief that one is dying nor yet the desire for death which comes from pain too great to bear Ryle who suffered from this evil symptom has left us the most exquisite description of this epitome of distress

As minutes lengthen into hours the pain continues No posture of rest nor restless movement softens its acerbity which when left untreated may itself overwhelm and kill its victim or so it appears Syncope may provide respite from pain as a too acute awareness ebbs and flows With or without therapy for pain the patient soon may begin to show signs of shock—yawning sweating thready pulse low or falling blood pressure a grey cyanotic color Or congestive failure may vie with shock for mastery of the victim Or early complications anuria hiccough or ileus may add torment to torment

Such then is the typical acute attack which may go on to a therapeutically guided convalescence unmarred by accident proceed into shock and early death or a stormy course may lead to recovery Heart failure may occur with or without arrhythmias Instant unforeseen death may bring down the curtain prematurely

The physical examination in acute myocardial infarction has no specific features and no pathognomonic sign The heart is apt to be enlarged the pulse fast often with extrasystoles or paroxysms of fibrillation of the atria or transiently of the ventricles Heart sounds are weak and distant a diastolic gallop common and a new murmur may be heard or a known murmur especially the murmur of aortic stenosis may disappear Arterial blood pressure usually falls but it may hold steady or even rise After the first day moderate fever is common and may last several days

Leucocytosis elevated blood urea nitrogen fast sedimentation rate transitory glycosuria and hyperglycemia may mark the first few days of the attack Though these abnormalities recognized by laboratory tests are tried and true and in the aggregate are helpful clues in prognosis it appears that the increased levels of glutamic oxaloacetic transaminase test introduced by LaDue Wroblewski and Karmen[34] are related more closely to the extent of acute muscle damage and thus statistically to prognosis The main trouble is that while statistics help us evaluate trends they don t tell us how John Smith will do A sudden asystole ventricular fibrillation embolus or rupture of the heart may end abruptly the most favorable course while another will survive almost every accident and bad sign

The electrocardiogram on which depends our nearest knowledge of the state of special parts of the heart muscle and all the arrhythmias has contributed a large part of our comprehension of myocardial infarction It must be learned in detail along sound lines of basic principles and evaluated in the light of clinical findings and those at autopsy It is not to be used as a cook book to bracket a diagnosis Its relation to coronary artery disease is considered elsewhere

CLINICAL MASQUERADES OF MYOCARDIAL INFARCTION

Myocardial infarction may elude the most conscientious and wise clinician He may not be able to penetrate its numerous disguises Or he may be misled by his interpretation of pain The commonest clinical masquerade of myocardial infarction is (1) *congestive heart failure* An acute infarct of the heart may manifest itself clinically in overpowering and prostrating left ventricular failure with the anguish of pulmonary edema The violent fight for breath occurs as a substitution symptom for pain or is itself so distressing that the pain is little noticed or neglected in the patient s description of his feelings while he is seen and forgotten in his recollection of his feelings later A bout of pulmonary edema whether treated or not may go on to established congestive heart failure Also those who have already had congestive failure may have a sudden sharp exacerbation as the clinical counterpart of myocardial infarction Sometimes one finds at autopsy a recent infarct whose epoch of origin was marked clinically by nothing more than the gradual and insidious development of congestive failure At times congestive failure occurs early where the diagnosis is established by a characteristic onset with pain or later on when convalescence had seemed well established

The (2) *neurologic masquerade* is one which for a long time lay buried under the mistaken assumption that acute cerebral disorders associated with myocardial infarction had to result from emboli or unrelated intercurrent acute thrombosis or hemorrhage More than 20 years ago when I surveyed a large series of cases of myocardial infarction proved at autopsy it was observed that hemiplegia which followed infarction of the heart was frequently associated with cerebral arteriosclerosis with no acute cerebral vascular lesion Local thrombosis or hemorrhage were found more often than an embolus Later Reed and I reported a series of cases in which *hemiplegia* was the presenting symptom of acute myocardial infarction There was one example of a severe epileptic convulsion as the clinical equivalent of the acute process of infarction with its hemodynamic and reflex changes The explanation is that if a person has severe but not occlusive cerebral arteriosclerosis any acute disturbance which reduces the flow of blood to the brain may produce clinical manifestations of acute cerebral ischemia The localization of signs depends on the areas of the brain where the blood supply is most seriously reduced If the maximal blood flow to the brain barely takes care of basal requirements anything which reduces cardiac output is reflected in a clinical state which may include hemiparesis hemiplegia paresthesias convulsions or a bizarre mental state with stupor mania or confusion Autopsy reveals no acute change in the cerebral

blood vessels but the ancient evil of well established arteriosclerosis with irregularities and narrowings. There is acute myocardial infarction even though the patient complained of no pain and had all the clinical findings of apoplexy. While it is necessary to have an autopsy to get final proof of this syndrome no doubt many less severe degrees of the same process occur. Suspicion that the heart may be the seat of the mischief should allow one to make the proper diagnosis by taking an electrocardiogram.

The third variety of masquerade may be a situation in which an all pervading weakness (3) an *overwhelming acute depression of mind and body* an ill defined but sometimes terrifying fear or anxiety may occur during acute infarction without there being any sense of pain whatever. Occasionally hyperventilation occurs under such circumstances.

A (4) *syncopal attack* which may wax and wane as it merges with shock and coma sometimes ushers in myocardial infarction. Faints and fits may occupy the whole of the picture or occur as episodes. Syncope and a story of previous faints may suggest an added risk of sudden death.

The clinical picture may be a complete blank a vacuum of signs or symptoms. Apparently healthy persons who have had careful medical supervision may die of something else or be killed. A large well healed scar or even a fairly recent infarct may be found. There may be a vague history of some meager indisposition or only serene health. Not yet can we claim full agreement of symptoms signs and lesions in coronary disease.

CLINICAL COURSE AND COMPLICATIONS

The clinical course after an acute myocardial infar
next to
elusive a
may occur early during shock at any time from ventricular fibrillation or sudden syncopal death. Embolic accidents are a hazard after the first few days and miscellaneous intercurrent thromboses or hemorrhages may occur throughout the course of the disease.

Congestive heart failure may be part of the clinical onset or it may make its appearance during convalescence. During the early days one encounters fever tachycardia various arrhythmias elevated white count sedimentation rate blood urea nitrogen and a conspicuous rise in the serum transaminase. These factors are summarized in Figure 1. Blood pressure as a rule tends to fall and not to regain the levels that had existed prior to infarction of a substantial area of heart muscle. There may however be an elevation in blood pressure especially during the early stages of the attack or the blood pressure may stay at approximately the preinfarction level whether this was in normal or hypertensive ranges. Pericardial friction rub may be heard anytime during the first two weeks but is by far more common during the first second and third day and thereafter may appear for the first time and reappear during the second week. It will be heard more often if it is looked for repeatedly. Congestive failure may begin insidiously or may occur with bouts of pulmonary edema even when these did not occur during the early stages of infarction. Gallop rhythm is a common finding. Fluoroscopic examination may reveal no pulsation of the left ventricle or a systolic expansion. Later a ventricular aneurysm may develop.

If a patient has withstood the first onslaught of myocardial infarction has endured the pain survived the shock recovered from congestive failure if it appeared the question is "What then?" Here is a systematic list of the important potential complications which may mar an otherwise smooth course. (1) There may be an extension of the thrombosis and thus a spread of the infarct. This was rare or rarely noticed until it was brought forward as another reason for using anticoagulants. (2) Arrhythmias which ordinarily begin with multifocal ventricular extrasystoles may give rise to ventricular tachycardia which in turn may merge into ventricular fibrillation. This the counterpart of asystole is fatal unless immediately reversed. But anyone who has had a heart attack and whose attention has necessarily been settled on the organ which symbolizes life and which indeed must function smoothly for life to continue may be plagued

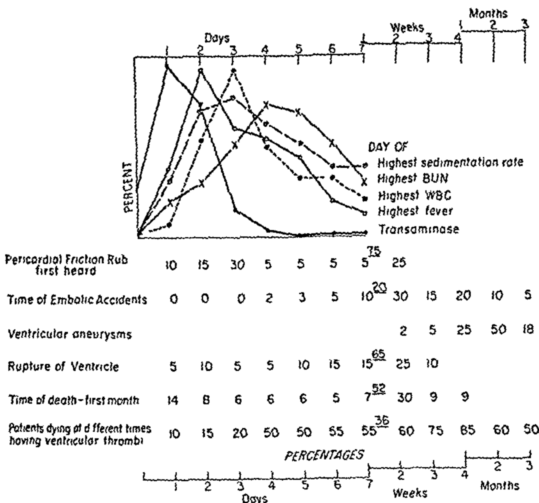


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and tormented by palpitations extrasystoles and anything which calls his fearsome and unwilling attention to his heart To this then may be added (3) anxiety so that the whole symptom complex even if most favorable from the point of view of repair of the heart without hemodynamic accident or episode may wind up as a cardiac neurosis The gloom and foreboding often enough lead to (4) a depression which may arise so imperceptibly out of the last stages of convalescence that it goes unrecognized until the patient is demoralized or even commits suicide (5) Congestive heart failure may begin to develop only during the period of convalescence It may have been present before and recur days weeks or months after the original attack Its advent may herald the acute onset of infarction Congestive failure may arise so insidiously that it becomes obvious only after the patient begins to resume or has resumed normal activity It may commence as another acute paroxysm of left ventricular failure and pulmonary edema in which event it may signify a sudden strain on the heart or a new myocardial infarct or an extension of an old infarct It is well to remember that not all clinical episodes of pain or congestive failure mean that the heart has

suffered new infarction If congestive failure becomes established its manifestations are those of congestive failure associated with hypertension or valve disease Pulmonary edema cyanosis and engorgement of the neck veins painful distention of the liver peripheral edema ascites all may occur in varying degrees The problem of sodium retention may be distressing The therapy is the same as for other forms of congestive failure which is discussed elsewhere Occasionally renal failure with azotemia may occur Jaundice usually but not invariably signifies pulmonary infarction in the presence of congestive failure

(6) Angina pectoris may appear de novo after myocardial infarction Having existed before it may continue In an occasional patient a myocardial infarct apparently puts out of business the sensitive area in nerve artery and muscle from which the stimuli arose in the past so that one may have the happy experience of a clinical episode of infarction of the heart bringing relief from anginal attacks This respite however is ordinarily bought at a considerable price Few patients survive long after such a train of events

(7) Episodes of minor shock syncopal attacks fainting dizziness orthostatic hypotension sweating and numerous vasomotor responses recur during convalescence Many of them are probably not different from what has been found in healthy people who are forced to remain in bed for a time But after the shattering experience of being laid low by a "heart attack" these signs and symptoms may be magnified and obsess the patient A profound neurosis may occur

(8) Rupture of the heart may dramatically and not altogether unexpectedly ring down the final curtain The epoch of rupture lasts for the first two weeks with perhaps some increased danger towards the end of the first week (see Fig 1) Rupture may occur up to the end of the first month though so late an event suggests a fresh infarct or extension of the original one Very rarely there may be rupture of an aneurysm though ordinarily rupture is a hazard only during the period of convalescence from an acute myocardial infarct Survival after rupture falls into four categories (A) There may be instant syncopal death (B) The majority of patients die a few minutes after what seems to have been the actual rupture with acute tamponade inflow stasis sudden venous engorgement cyanosis severe respiratory embarrassment and evidence of cerebral anoxia (C) Another group includes those who survive for one or several hours because the rent in the ventricle is small and it takes some time for enough blood to leak out to produce fatal tamponade (D) An occasional patient survives for many days perhaps with development of a false ventricular cavity in the pericardial space with endothelialization

(9) Ventricular aneurysm will be detected in proportion to the assiduousness of the search as well as the criteria for its diagnosis While physical signs may be suggestive it can be demonstrated only by x ray or at autopsy

(10) The hand shoulder syndrome is likely to occur as a delayed sequel several weeks after myocardial infarction or it may put in its appearance only after convalescence seems to have been completed Ordinarily the elbow is relatively free from pain which may be confined to the shoulder or occur in the hand and shoulder The nature of this complication is not clearly understood Some orthopedists believe it to be completely circumstantial in its association with myocardial infarction Certainly similar patients may be seen who have had no myocardial infarction It may occur in people who have had angina without any classical attack of myocardial infarction and occasionally it occurs in congestive failure as well as in a miscellaneous assortment of patients Cardiologists and internists are likely to see it most often after myocardial infarction In my opinion it does bear some specific relationship to myocardial infarction in many cases though what the connection is we do not know The best current concept is that it is a vasoneurosis related to traumatic vasospastic states such as Sudek s atrophy Sympathectomy has been less successful in treatment than has the use of steroid hormone therapy The condition itself unless treated may be demoralizing as well as disabling

(11) Pericarditis with its evanescent friction rub and occasional electrocardiographic components is another sign which usually has

no specific symptom connected with it. It will be found only if the heart is examined several times a day and may come and go for a few days. As another index of severity it adds its small weight on the side of an unfavorable prognosis.

(12) Extracardiac embolism and infarction constitute the major clinical hazard. They are unpredictable. There is no clue by which one can make a diagnosis of ventricular mural thrombus. In the presence of congestive failure, thrombi may occupy the atria and auricles. Fibrillation of the atria seems to favor the existence of a thrombus more than its dislodgement, though it is very difficult to get true insight into such matters even by post mortem studies. There is evidence that during myocardial infarction increased coagulability of the blood exists. This, together with the shock which ensues, may account for the surprisingly high incidence of simultaneous or associated extracardiac thromboses in artery and vein. Immobilization in bed adds to the frequency of venous thrombosis in the lower extremities. There is not yet evidence to determine what may be the added risk of (13) anticoagulants in producing hemorrhage into the wall of the coronary artery leading to coronary occlusion, reabsorption of the original thrombus, or dislodgement of the thrombus which provides the substance of the embolism. There may be some small coronary vasodilator effect.

(14) Dressler has recently described what he calls a post myocardial infarction syndrome which consists of pericarditis, pleurisy, pneumonitis, singularly or together, protracted fever and pain with friction rubs, and x-ray evidence of pleural and pericardial effusion, cough, rales, and pulmonary infiltrates with an increase in the white count and a sedimentation rate characterizes the picture. It may last for many months. The exact nature is not known and it is not known whether there is anything specific about it or simply that this kind of pattern may occur after myocardial infarction.

(15) Symmetrical peripheral gangrene has been described elsewhere as a possible complication in myocardial infarction. It has some relationship to livedo reticularis and mottled cyanosis and erythema of the skin which may occur under a variety of conditions in which peripheral circulation is impaired or threatened. As such it is a bad omen.

TREATMENT

In the early days as our understanding of the clinical significance of myocardial infarction was beginning, the physician had little more than absolute rest to recommend to his patients, treating the shock with transfusions and supportive measures. He might correct congestive failure if he could overcome his fear of digitalis. The traditional reluctance to use digitalis came from the fact that many people who have had myocardial infarctions and were treated with digitalis died. There is abundant evidence to suggest that they die not of the digitalis but of the congestive failure and the underlying disease. Today the patient with infarction of the heart should be treated with digitalis whenever he has congestive failure, realizing that the prognosis is poor but is worse without proper treatment of the heart disease.

Death after acute myocardial infarction may come from (1) shock, (2) arrhythmias with cardiac standstill, ventricular fibrillation, or "instant physiologic death," (3) congestive heart failure, (4) thromboembolic accidents, or (5) miscellaneous unrelated conditions. There has been a substantial breakthrough in therapy for myocardial infarction in three places which have reached significant importance during the last decade. These consist of the use of anticoagulants to help reduce the incidence and severity of thromboembolism, the use of norepinephrine to combat shock, and a relaxation of the sentence to absolute rest, now culminating in such methods as the "arm chair" treatment of coronary thrombosis.

The treatment of acute myocardial infarction must be tailored to fit the individual patient. The first consideration is to make the patient comfortable. This is done by allaying pain with morphine, demerol, codeine, or some combination, and by calming anxiety. Though morphine often serves this end, the patient tormented by pain, feeling that his life is

threatened, as it may well be, needs the reassurance and comfort that a wise clinician can bring. If the patient's confidence can be gained, an important phase of the battle has been won. For in addition to uneasiness, restlessness, and purposeless movement, anxiety often leads to hyperventilation with all the unpleasant and undesirable cardiorespiratory effects to add to the general difficulty. Shock may require heroic therapy. Norepinephrine may be added in varying amounts to an intravenous infusion of 5% of dextrose, care being taken to avoid letting the material get out of the vein into the tissues. Not only does the response of each individual patient have to be titrated but there may be a good deal of variation in response over a period of 24 hours. An effort should be made to maintain the systolic blood pressure around 100 mm. Hg though it should be kept around 120–130 in previously hypertensive patients. Part of the adjustment may be obtained in increasing the rate of flow of infusion, but this should not exceed 40 drops a minute, so the concentration may be increased.

Oxygen should be given if needed. Associated pulmonary edema should be treated appropriately, sometimes by venesection or the application of tourniquets, rotated in succession, and the use of oxygen with alcohol or antifoaming agents if the facilities are available.

The principle that a damaged organ needs rest while it repairs itself has not been outmoded by the invention of arm chair therapy, though this has been very helpful where it has been used in accordance with varying circumstances. Having a certain amount of freedom without absolute rest may help relax the patient's fears and allow his circulation to adjust to a more normal form of existence. However, sitting upright may be extremely tiresome, particularly in the early stages of the disease. It should not be forced, nor should it be extended beyond the period when it grows tiring. Much medical lore has grown up around the bedpan. If the patient is able to use the bedside commode with assistance, it has many advantages. Each patient must be individualized. A former student of mine in India tells me that his patients enjoy total invalidism and will have no part of arm chair therapy.

To the catabolism which the death of heart muscle produces, enforced rest in bed adds an element through humeral mechanisms not yet completely understood. For this reason, it is important to pay careful attention to diet, fluids, salt intake, and the proper functions of elimination. When the patient is very sick, he obviously will not want to eat much. Small quantities of various fluids such as milk, fruit juices, tea, broth, water may be used varying the situation according to the state of the patient and his wishes. As soon as convalescence is established we add soft foods such as poached or soft boiled eggs, puddings, stewed fruits, cooked cereals, potatoes and small portions of well-chopped beef. Gradually a normal diet should be resumed, though greasy foods and those which are hard to digest should be eliminated unless the patient has a special interest in them. Salt restriction may be necessary if the patient has congestive failure or is threatened by it. The use of coffee, tea, and alcoholic beverages again must be individualized, though there is little indication that any of them does any good which can be measured pharmacologically. Their customary employment may indicate to the patient that the stormy part of the voyage is over and the harbor in view. Even most heavy smokers do not feel much like smoking shortly after an acute myocardial infarct. The problem comes up during convalescence. The meaning of the relationship of heavy smoking and coronary artery disease in an ageing population with variable degrees of correlation is difficult to interpret as cause and effect. Smoking may soothe the jangled nerves of citizens of a jittery nation and culture. To the extent that smoking in moderation is possible it may avoid an additional frustration. For many people, a myocardial infarct is a reasonable milestone for stopping. I have not found that my stern orders, suggestions or encouragement were effective in getting most patients to stop or even to moderate smoking.

Anticoagulants

Despite the difficulty of getting unequivocal

idence even by our best statistical approaches to an evaluation of anticoagulant therapy the bulk of the testimony indicates that we should accept the definite added risk which anticoagulants bring because anticoagulants appear to be effective in (1) reducing the mortality (2) reducing the frequency of embolic accidents (3) reducing the incidence and extent of spread of the initial thrombus and (4) perhaps shortening the period of convalescence Anticoagulants can be given only where a reliable laboratory can provide daily estimates of prothrombin This provides a measure of safety against hemorrhagic accidents on the one hand and failure to achieve relative intracoagulability of the blood on the other A vexing problem for which there is at present no final answer is whether in the very mild case anticoagulants should be given at all Of course the problem hinges on an interpretation of the "mild case and whether or not there is such a thing as a good risk patient In my own experience I have not used anticoagulants in good risk patients Some of my colleagues have So far there is no indication that one method is better than the other but we have seen too few for a statistical attack upon the problem A valuable byproduct of the use of anticoagulants is to require very close attention to the patient by his physician and the hospital staff No one has as yet evaluated to what extent such attention influences morale favorably and permits any complication to be detected early and treated if there is a treatment The difficulty of treating patients with infarction has been increased by this method This is no justification for omitting it Further effort should be encouraged to search for a simple bedside method which would give a true estimate of the coagulability of blood The clotting mechanism is vastly more complicated than our original formulations suggested so this simple desideratum may never be reached

The actual administration of anticoagulants should follow a consistent plan so that experience will give the necessary familiarity If the coagulation of the blood is normal depository heparin 2 3 or 400 mg are injected intramuscularly and simultaneously 300 mg of dicumarol are given by mouth On the second day 200 mg of dicumarol are given and if the prothrombin time has not been influenced adequately 200 mg of heparin may be given at the same time The oral anticoagulants are then continued so as to keep the prothrombin time between 2 and 2 5 times that of the control value By the Quick method it should range somewhere between 25 and 35 seconds with a normal of 13 Many of the newer anticoagulants are effective but there are no very extensive studies of comparing the advantages and disadvantages of the various methods Close watch should be made repeatedly for any unusual bruising purpura or actual hemorrhage This demands that the anticoagulants are to be stopped at once phytonadione injected slowly 50 mg within a period of 3 to 4 minutes Ten mg may be given orally if it is planned to resume therapy when hemorrhage ceases though this is very risky because of the hazard of internal hemorrhage One point must always be kept in mind in the employment of anticoagulants That is to achieve any therapeutic value at all one has to reduce the coagulability of the blood By so much as it is reduced the problem of hemorrhage is introduced so that one in treating exchanges or hopes to exchange a controllable disease process for one which is itself not otherwise controllable The best we can hope for is to reduce such complications as new thromboses and embolization rather than to repair the damage already done There has been slight but definite increase in the frequency of hemopericardium after myocardial infarction Bleeding comes from a diffuse seepage through the infarcted area leading to hemorrhagic tamponade rather than actual rupture of the ventricle though that may happen too In experimental animals rupture is not more likely to occur after anticoagulants have been used than without them

The treatment of congestive failure and arrhythmias is considered in the appropriate section The fact that they occur in patients with myocardial infarction should not in itself change therapy

AUTOPSY FINDINGS

The pathological findings after death from

myocardial infarction depend upon many factors such as presence and degree of hypertension, diabetes, and site and localization of *arteriosclerosis with attendant disease of kidney*, brain and extremities, and many other factors The actual state of the myocardium will depend upon the presence of concurrent disease and the particular anatomical arrangement of the infarct This is influenced by the physical arrangements of the muscle bundles, the location and degree of arteriosclerosis, the presence and extent of actual coronary thrombosis if it is present All these will be modified by the size and extent of collateral channels

Hypertrophy of the heart is found in about 80% of the people dying with myocardial infarction The most important factors are hypertension and previous congestive failure In patients who have never had hypertension or congestive failure however, the heart may be enlarged in those who die of an infarct *Intracardiac mural thrombi* are most common in the left ventricle just as anterior and apical infarction is the most common site for the underlying lesion Also there may be mural thrombi in the atria, particularly after long congestive failure, dilatation of the atria or fibrillation Since there is no way to make a diagnosis of mural thrombus during life, it is not possible to say always what the fate of such clots may be Some probably are more or less completely resorbed, some break off and form emboli, and it is the belief of some pathologists that a few may undergo a myxomatous transformation and be mistaken for true myxomas though this must be exceedingly rare Figure 1 gives the pertinent findings with reference to the formation of mural thrombi and the development of extracardiac *embolism* The incidence of *ventricular aneurysm* depends very largely on the kind of clinical material from which the figures are drawn Since it is unusual in the early stages a series with many early deaths would have relatively few ventricular aneurysms It is important not to mistake a cardiac aneurysm for pericardial effusion and introduce a needle to aspirate fluid with disastrous results Rupture of *aneurysms or rupture* of a well healed scar is rare but may occur Occasionally a myocardial infarct may heal with formation of calcium and very rarely actual bone formation has occurred thus justifying the ancient folk belief in hardness of heart

Spontaneous *rupture of the ventricle* usually involves the apex of the left ventricle More rarely the septum and still more rarely a papillary muscle may be ruptured or a tendinous cord may pull loose from its moorings in the ventricular wall *Infarcts of the auricle* may occur, and not nearly as rarely as was thought formerly since they seem to be found with increasing frequency when they are searched for *Pericarditis* is ordinarily localized to the area overlying the infarct Occasionally it may be generalized and presumably there is some additional etiologic mechanism in such cases Pericardial effusion is usually associated with *congestive heart failure* and of course the signs of anasarca, peripheral edema, ascites and hydrothorax, particularly right-sided hydrothorax, are findings which occur where congestive failure has existed for a time Cerebral vascular lesions may be thrombotic or hemorrhagic as well as embolic, and the various destructive elements of peripheral embolization from ventricular mural thrombi are not different from those caused by other mechanisms *Pulmonary infarction* is common in congestive failure and often arises from thrombosis of pulmonary veins or branches of the pulmonary artery Emboli from right ventricular mural thrombi lodge in the lungs Massive pulmonary embolus is usually a sequel to thrombosis in one of the systemic veins rather than from mural thrombosis *Coronary* arteriosclerosis has been discussed elsewhere.

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HAPTER 31

Diseases of the Aorta and Cardiovascular Syphilis

Ernest O Theilen M D

CONGENITAL MALFORMATIONS OF THE AORTA

VASCULAR RING ANOMALIES

Early in embryonic life six pairs of aortic ches develop The first second and fifth airs soon disappear The third arches be- ome the carotid arteries and the right fourth ch forms the innominate artery The fourth ft arch persists as the arch of the aorta The xth arches give rise to the pulmonary arteries nd the ductus arteriosus Arrested develop ment or disappearance of portions of the em ryonic arches as well as persistence of those hich are usually obliterated can produce a ide variety of abnormalities Vascular ring nomalies are not as a rule threatening to life nd often are asymptomatic They may pro uce difficulty however by compressing either he trachea or esophagus A right sided aortic rch is the result of disappearance of the fourth eft arch and persistence of the fourth right rch is commonly associated with a right de cending aorta and is usually asymptomatic Occasionally a dilated right aortic arch may produce paralysis of the right vocal cord be ause of pressure on the right recurrent laryn eal nerve X ray examination shows the aortic knob to the right of the sternum It may be somewhat obscured by the superior ena cava which is displaced to the right The esophagus lies to the left of the aorta and is indented to the left in the anterior posterior projection The ligamentum arteriosum may pass from the pulmonary artery to the left of the trachea and behind the esophagus to join the aorta thus encircling the trachea and esophagus Symptoms of compression of these structures include dyspnea cough stridor and dysphagia A right aortic arch can be asso ciated with a left descending aorta In this situation the aorta crosses to the left behind the esophagus and can be visualized on x ray examination with barium as a posterior pulsat ing filling defect in the esophagus A double aortic arch is formed when both fourth arches persist The double arch forms a ring around the trachea and esophagus and commonly pro duces symptoms Stridor and dysphagia may occur in infancy and may be severe Infants with tracheal obstruction due to a double aortic arch tend to hold their heads in hyper extension Flexion of the head on the chest may significantly increase the obstruction It is not unusual for respiratory distress to in crease transiently during the act of swallowing Physical examination may reveal the use of the accessory muscles of respiration as well as intercostal and suprasternal retraction Gen erally one of the arches is smaller than the other the smaller one may not be patent for its entire length Obstructive symptoms can be relieved successfully by division of the ligamentum arteriosum when it exists with a right sided arch or by division of one of the arches in case of a double arch

An anomalous right subclavian artery arises from the left aortic arch and crosses to the right behind the esophagus A similar situa tion can exist for the left subclavian artery in case of a right sided aortic arch The presence

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is too long to permit an end to end anastomosis after resection an aortic graft or prosthesis is used As a rule the optimal time for surgical intervention is between the eighth and fifteenth years of life If possible operation is postponed in the very young until collateral circulation has had time to develop Surgery may be necessary at an earlier age if symptoms are severe or progress rapidly or if cardiac failure develops If collateral circulation is inadequate cross clamping of the aorta for more than a few minutes can produce spinal cord ischemia with permanent damage The use of hypothermia permits a longer period of interruption of the circulation Surgical intervention much beyond the twentieth year of life becomes increasingly hazardous because of sclerotic changes in the aorta which interfere with its ability to hold sutures

AORTA PULMONARY ARTERY COMMUNICATIONS

Of the various communications between the aorta and the pulmonary artery the most common by far is the patent ductus arteriosus Defects in the septum between the aorta and the pulmonary artery just above the semilunar valve or adjacent to the right aortic sinus are rare These defects can be mistaken for a patent ductus because of the similarity in clinical signs Patent ductus arteriosus truncus arteriosus and transposition of the great vessels are usually considered with other congenital lesions of the heart and will not therefore be discussed at length in this chapter except to re emphasize the importance of recognition and treatment of the patent ductus Even though a patent ductus does not necessarily interfere with growth and development and may remain asymptomatic for many years the long term outlook is distinctly unfavorable The average age at death of unoperated patients is approximately 35 years Subacute bacterial aortitis usually on the pulmonary side of the ductus is common One of the greatest hazards however is the development of severe pulmonary hypertension and irreversible pulmonary artery changes which may contraindicate an attempt at closure of the ductus

ATHEROSCLEROSIS OF THE AORTA

Atherosclerosis together with other forms of arteriosclerosis is the most common degenerative disease and is one of the most important causes of death at the present time It is almost universal in the aged Unfortunately it begins to make its appearance fairly early in adult life particularly in men Despite extensive experimental work the etiology of atherosclerosis in man has not been determined with certainty The evidence for the deleterious effects of excessive dietary fat is impressive but the question has not been proved Hypertension very likely accelerates the formation of atheromatous deposits but is not the sole factor Pathologically the process begins with the deposition of cholesterol in the intima both intra and extracellular Much of the lipoid is contained in macrophages which ultimately degenerate The lipid deposits are associated with fibrous proliferation in the subintima The intima and the endothelium become thickened Calcium is deposited in the scarred areas The media may also be involved with atrophy of the elastic tissue and fibrosis It is the medial changes which are responsible for the development of arteriosclerotic aneurysms However dilatation and elongation of the aorta are the most common results of these changes The elongation of the aorta increases the tortuosity of the vessel which may not be detected except on x ray examination Although the elongation may actually produce buckling of some of the vessels arising from the arch of the aorta the buckling usually is not associated with symptoms Extremely tortuous vessels such as the innominate may be confused with aneurysms Although arteriosclerotic aneurysms can occur at any point along the aorta they are much more common in the abdominal aorta below the origin of the renal arteries and frequently occur just above the aortic bifurcation Fusi

of such a vessel can be demonstrated radiographically by a posterior indentation of the barium filled esophagus Most of these are asymptomatic but occasionally dysphagia is present This may occur relatively late in life and only after the aberrant vessel has become dilated and tortuous as a result of arteriosclerosis

COARCTATION OF THE AORTA

Coarctation of the aorta is a partial or complete developmental constriction usually in the descending aorta The constricted segment may be very short or there may be hypoplasia or atresia extending for several inches Coarctation above the level of the ductus arteriosus and terminating at the insertion of the ductus is referred to as the infantile type Collateral circulation is poor in this particular situation and the ductus usually remains patent with characteristic cyanosis of the lower half of the body because of shunting of blood from the pulmonary artery into the aorta This anomaly is not generally compatible with long life if the coarctation severely restricts blood flow to the distal aorta Death may occur in the first few weeks of life from congestive failure Treatment is generally unsatisfactory for this type of coarctation

The more common location for coarction designated as the adult type is usually just distal to the attachment of the ligamentum arteriosum to the aorta Coarctation does occur in the descending thoracic aorta beyond this point but is uncommon Dilatation of the aorta proximal and distal to the site of the coarctation is common Atherosclerotic lesions are frequent in the same location Young children usually do not show the development of many collateral vessels particularly if the constricted segment permits a fairly high flow of blood In most adults however there is an extensive network of collateral vessels proportional to the severity of the coarctation Bicuspid aortic valves are associated with coarctation in approximately 40% of the cases

Coarctation is by no means a benign condition The average age at death is approximately 30 years Symptoms in the adult type of coarctation result from the hypertension which exists in the arterial compartment above the coarctation and to the reduced flow in the lower extremities Symptoms are often lacking during childhood and physical development may be entirely normal Weakness of the legs during strenuous physical activity may be noted and effort pain occurs as well The hypertension above the coarctation may be associated with headaches and dizziness cerebral hemorrhages occur Angina pectoris develops occasionally in older patients and cardiac failure is not uncommon Rupture of the aorta can occur as well as dissecting aneurysms which begin either proximal or distal to the site of the coarctation Sudden death from rupture of the aorta accounts for slightly less than one fourth of all fatalities The average age at death following rupture of the aorta is slightly less than 30 years Subacute bacterial endocarditis or bacterial aortitis takes a heavy toll Formerly this accounted for about 20% of the deaths

Physical examination in the adult type of coarctation will reveal diminished to absent pulsations in the femoral vessels Hypertension exists in the arms Although the systolic pressure is reduced in the legs the diastolic pressure is often at normal levels Dilated tortuous intercostal arteries are often palpable Pulsations may be seen on the back and shoulders when the patient leans forward Systolic bruits are usually heard best to the left of the spine between the scapulae but often are audible to the left of the sternum as well X ray is the most useful laboratory tool for establishing the diagnosis One of the most helpful signs is the presence of notching along the lower border of the rib margins caused by erosion of the ribs by the tortuous intercostal vessels A notch in the left border of the descending aorta at the level of the main pulmonary artery may also be seen Retrograde aortography is valuable in delineating the exact site and extent of the coarctation

The treatment of choice for coarctation is resection of the constricted segment with an end to end anastomosis This is not always possible Sometimes as a compromise an end to side anastomosis between the left subclavian artery and the aorta distal to the coarctation is made If the constricted segment

is too long to permit an end to end anastomosis after resection an aortic graft or prosthesis is used As a rule the optimal time for surgical intervention is between the eighth and fifteenth years of life If possible operation is postponed in the very young until collateral circulation has had time to develop Surgery may be necessary at an earlier age if symptoms are severe or progress rapidly or if cardiac failure develops If collateral circulation is inadequate cross clamping of the aorta for more than a few minutes can produce spinal cord ischemia with permanent damage The use of hypothermia permits a longer period of interruption of the circulation Surgical intervention much beyond the twentieth year of life becomes increasingly hazardous because of sclerotic changes in the aorta which interfere with its ability to hold sutures

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form aneurysms are more common than saccular aneurysms In many instances atherosclerosis seems to develop first near the bifurcation or at least the lesions are more extensive in that location probably because the aortic wall in this region is subject to greater impact and higher pressures during systole than at more proximal locations Summation of the forward pressure wave and the reflected wave from the bifurcation produces a higher systolic peak

The chief symptom of abdominal aortic aneurysms is deep seated aching pain which may be referred to the abdomen back or both It occurs on the left side more frequently than elsewhere Physical examination reveals a mass in the abdomen usually to the left of the spine it is often pulsatile and sometimes tender On x ray examination the wall of the aneurysm is frequently outlined by calcareous deposits Vertebral erosion is rare Rupture of arteriosclerotic aneurysms is accompanied by excruciating abdominal or back pain and signs of hemorrhagic shock Rupture can terminate in sudden death or the bleeding may be slow and chronic Some aneurysms can be resected and continuity restored by replacement with an aortic homograft or a prosthesis

When atheromata destroy the endothelium ulcerations form which predispose to thrombosis Most thromboses are not extensive enough to interfere with blood flow, but occasionally they can occlude vessels and this produces symptoms Thrombosis may develop initially in an iliac artery and propagate retrograde into the aorta Leriche in 1940 described a syndrome of chronic occlusion of the aorta at the bifurcation It is now apparent that this entity is much more common than was realized a few years ago It occurs primarily in men from 40 to 60 years of age The disease is characterized by a well localized occlusive process in the terminal aorta and bifurcation It is insidious in onset and the symptoms are those of slowly progressive arterial insufficiency Pain and muscle fatigue in the hips and legs are common One of the presenting complaints may be sexual impotency On examination the femoral pulses are absent Collateral circulation develops to a variable degree and may prevent trophic changes in the skin although pallor of the legs and feet is common This is in contrast to the trophic changes which occur in a leg when thrombotic occlusion involves an iliac artery only Treatment consists of endarterectomy or resection of the aortic bifurcation and replacement with a prosthesis Experience with homografts has not been satisfactory Degenerative changes occur and aneurysms may form Gradual occlusion at the graft site sometimes develops

DISSECTING ANEURYSMS

Dissecting aneurysms of the aorta are separations of the layers of the aorta accompanied by hemorrhage within the vessel wall and frequently associated with tears in the intima as well as rupture of the external layers of the aorta This uncommon but dramatic disease is almost always fatal The incidence is higher in men than women particularly after the age of 40 They may occur in younger people however particularly in association with Marfan's syndrome coarctation of the aorta and pregnancy

Dissecting aneurysms can properly be considered as a separate entity Although arteriosclerosis and hypertension may be contributing factors in their development they are not the primary etiologic agents Syphilis cannot be implicated since the basic pathologic process in syphilitic aortitis is one of fusion rather than of separation of the layers of the media Originally dissecting aneurysms were thought to be secondary to tears of the intima in a sclerotic aorta with separation of the layers of the aorta by blood forced through the break in the intima This may be true in rare instances but in a surprisingly large number of cases the tear does not occur at the site of an atheromatous plaque and there is not necessarily an associated hypertension At the present time medial degeneration with necrosis often cystic is considered to be the basis of the disease process Bleeding from the vasa vasorum accounts

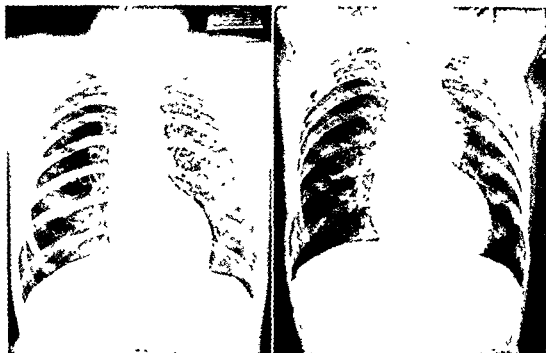


Fig 1 Dissecting aneurysm of the aorta in a 46 year old man with excruciating 'tearing' substernal pain and back pain The film at the left was taken 1 year before this illness The film on the right shows the widening of the aorta caused by the medial separation At autopsy two intimal tears were present with free communication between them

for the hemorrhage Many of the intimal tears are probably secondary to rupture of the intramural hematoma into the lumen of the vessel The majority of intimal tears occur in the ascending aorta and dissection also proceeds both proximal and distal to this point A proximal dissection can rupture into the pericardium with either acute or chronic tamponade Hemothorax, particularly on the left is also seen Retroperitoneal hemorrhage is less common The dissection often obliterates the ostia of vessels arising from the aorta with obvious symptoms of circulatory insufficiency Intimal tears may occur at both proximal and distal points along the aorta producing the so called gun barrel aorta Sudden death is not uncommon in this disorder, and the prognosis for survival is generally very poor and usually a matter of days at most

Dissection of the aorta is characterized by sudden severe excruciating pain which may be tearing burning, or constricting in character Although hypotension may occur, it is not the rule The pain is often mistaken for that of coronary occlusion and even acute pancreatitis or mesenteric thrombosis may be suspected It is most common in the anterior chest in the substernal region and does occasionally radiate into the neck Back pain is frequent Pain may migrate from the thorax to the abdomen With involvement of the abdominal aorta, pain may radiate into the legs Nausea vomiting, and diarrhea in abdominal aortic dissection may lead to an erroneous diagnosis of disease of the gastrointestinal tract Neurologic symptoms, particularly of spinal cord damage, but also occasionally of central nervous system ischemia occur as a result of interruption of blood flow to the spinal cord and brain by occlusion of the intercostal vessels or of the carotids by the dissection

Physical examination may reveal diminished or absent pulses in the radial, carotid or femoral vessels neurologic signs, and evidences of bleeding Signs of cardiac tam



Fig 2 Dissecting aneurysm of the aorta in a 78 year old man with sudden onset of chest pain and

dium were found

ponade or of hemothorax may be present Aortic diastolic murmurs occasionally are heard, probably as a result of distortion of the valve ring and of the cusps by the hematoma in the aortic wall Ecchymoses of the abdominal wall may accompany retroperitoneal bleeding but are not specific for dissecting aneurysms

Laboratory procedures are of little help in the diagnosis A normal electrocardiogram may be helpful in ruling out myocardial infarction Demonstration of progressive widening of the aorta in serial x ray films is sometimes of value (Figs 1 and 2)

Treatment at the present time is generally unsatisfactory

TRAUMATIC RUPTURE OF THE AORTA; TRAUMATIC ANEURYSMS

Rupture or less complete tears of the aorta can occur at any point and are not necessarily associated with penetrating wounds or even visible evidence of severe trauma to the external surface of the body Aortic injuries associated with trauma to the anterior chest wall commonly are found in the ascending portion or the arch Another of the common sites for this relatively rare aortic lesion is at the attachment of the ligamentum arteriosum or a short distance below it The heart is suspended by the pulmonary vessels and the arteries arising from the arch of the aorta The heart and aortic arch are relatively mobile within the chest but the descending aorta is more or less fixed just below the left subclavian Sudden deceleration causes excessive strain and tears at this point

Most of the aneurysms produced by trauma such as this are saccular and not infrequently the wall of the aneurysm is not composed of the thinned aortic wall but of connective tissue which has formed around extravasated blood

AORTIC ARCH SYNDROMES

The aortic arch syndromes are a rare group of disease entities characterized by absent or diminished pulses in the arms and neck as a consequence of narrowing or obliteration of the major vessels at their origin on the aortic arch These disorders have also been referred to as Takayasu s disease and pulseless disease Syphilitic aortitis was thought to be the etiologic agent in many of the earlier cases but it is not the only cause of this disorder Atheromatosis is rarely the major cause although it no doubt is a contributing factor at times Trauma has been suggested as a cause or as a precipitating factor Its precise role is difficult to evaluate Many of the cases of this disease are thought to be due to an arteritis the cause of which is unknown The incidence is somewhat higher in young women than in other groups

Most of the symptoms of this disorder are due to cerebral ischemia The cerebral manifestations include vertigo transient visual disturbances particularly with position change and during exercise headache syncope transient hemiparesis and hemiplegia

Physical examination will reveal diminished or absent pulses in the carotids and the brachial or radial arteries Frequently there is hypertension in the legs Trophic changes may be seen around the head including optic atrophy cataracts and skin changes Peculiar wreath like anastomoses around the optic discs have been described Systolic bruits and occasionally continuous murmurs may be heard over the upper sternum Pulsating collateral vessels over the back and evidence of rib notching occur Trophic changes in the arms do not occur because of the collateral circulation and also possibly because a fairly normal mean arterial pressure to the arms may be maintained although the pulsatile variations are damped out by the constrictions at the origins of the vessels

This disease must be differentiated from disorders such as the scalenus anticus syndrome which may be associated with trophic changes in the fingers and hands from aortic aneurysms with either delay or obliteration of pulses dissecting aneurysm embolism and blood vessel compression by mediastinal tumors Therapy is generally unsatisfactory unless syphilitic aortitis is present Thromboendarterectomy has been suggested as a possible approach but has not been evaluated adequately

CARDIOVASCULAR SYPHILIS

During the past decade there has been a decrease in the incidence of cardiovascular syphilis so that it now constitutes only a small percentage of patients with heart disease The introduction of penicillin in 1944 and its widespread use no doubt has been a major factor in the advances which have been made over the control of this disease The extensive use of serologic testing procedures as well as public health measures cannot be minimized Despite the advances which have been made syphilis is far from a vanishing disease and continued vigilance will be required to control it Decreased emphasis on syphilis as a public health problem and laxity arising from decreased awareness has probably led to complacency For each case diagnosed and reported many more undoubtedly go undetected and untreated The general physician and internist seeing patients with cardiovascular problems must consider syphilis in the differential diagnosis since failure to treat the disease early can lead to disaster

PATHOLOGY

Cardiovascular syphilis is primarily a disease of the arteries the myocardium is rarely involved The vascular lesions as a rule are most extensive in the aorta but other blood vessels may be involved Syphilitic aortitis is essentially a chronic cellulitis which usually begins in the ascending aorta a short distance beyond the aortic cusps and spreads from this site both proximally and distally The changes are most pronounced in the ascending aorta and in the arch they generally become less conspicuous in the descending thoracic aorta and as a rule gross lesions are uncommon below the level of the diaphragm In very early lesions involvement is most extensive in the adventitial layers of the aorta but later changes are seen in all of the layers Invasion of the aorta occurs by way of the perivascular lymphatics and is associated with a periarteritis An endarteritis is almost invariably present Patchy medial necrosis with destruction of the elastic tissue is one of the outstanding pathologic findings Healing takes place by fibrosis Irregular deposition of fibrous tissue occurs in the intima the thickened areas eventually undergo hyaline change and the surface becomes irregular furrowed and wrinkled The appearance has often been compared with that of tree bark The intimal lesions do not necessarily undergo atheromatous change although the two processes often are coexistent When the intimal changes occur near the coronary ostia a reduction in the size of these openings may occur This can lead to chronic coronary insufficiency and ultimately to coronary occlusion As a rule the arteritis does not involve the coronary arteries themselves Involvement of the aortic cusps without disease of the adjacent aorta is almost never seen A peculiar cord like thickening of the free margins of the aortic cusps often with some retraction of the cusps may occur as an extension of the aortitis Changes in the aorta near the insertion of the valve cusps may separate the commissures and lead to aortic insufficiency The destructive changes in the aorta may be more extensive in one area than in another and may so weaken the wall that local dilatation occurs Aneurysms form in this way When the weakening occurs in the region of the sinuses of Valsalva aneurysms may form here as well

Involvement of the myocardium with the production of a true syphilitic myocarditis is extremely rare and diagnosis is dependent upon the demonstration of spirochetes in the tissue Gummas of the myocardium do occur but are uncommon Rarely they may lead to a ventricular aneurysm

SYPHILITIC AORTITIS UNCOMPLICATED

It is not possible to give precise figures for the incidence of cardiovascular involvement in patients with syphilis because of variations in the criteria for diagnosis of the disease A fair estimate of the incidence of aortitis complicated and uncomplicated would be 10 to 15% of patients with syphilis Although the disease is more prevalent in males with the highest incidence between the fourth and fifth decades the interval from the initial infection to clinical recognition of cardiovascular involvement is more important The incidence of cardiovascular syphilis in untreated patients increases from the tenth year after the initial infection to reach a peak at about 20 years

Uncomplicated syphilitic aortitis implies the presence of demonstrable lesions which have not progressed to the point of aneurysm formation of obstruction of the coronary ostia or of aortic insufficiency Clinical manifestations may be lacking and generally the disease is asymptomatic Non radiating substernal pain of short duration not related to exercise has been said to be related to syphilitic aortitis but this symptom is by no means specific and its evaluation is quite difficult Systolic murmurs over the aortic area have been described and have been attributed to dilatation of the aorta A ringing timbour like quality of the aortic second sound is suggestive of aortitis but this sign loses all significance if there is arteriosclerosis or hypertension Physical signs alone are not diagnostic of uncomplicated syphilitic aortitis and undue emphasis should not be placed on them Radiographic examination is helpful if marked

dilatation or calcification of the ascending aorta can be demonstrated Calcification confined to the ascending rather than the descending aorta in relatively young people is highly suggestive of syphilitic aortitis Calcification in the same area in the aged does not have the same significance as in younger people since it can occur on the basis of arteriosclerosis alone Measurement of the width of the aorta alone can be misleading It must be emphasized that there are no pathognomonic radiographic signs of uncomplicated syphilitic aortitis Angiocardiographic examination is of limited value It will help in delineating the ascending aorta which otherwise cannot be well visualized but again the changes which are seen are not specific

SYPHILITIC AORTIC INSUFFICIENCY

Syphilitic aortic insufficiency is the most common complication of syphilitic aortitis It develops when as a consequence of the aortitis there is widening of the commissures with separation of the cusps Extension of the cellulitis into the valve cusps with retraction as well as cord like thickening of the free margins contributes to malfunction of the valve Aneurysmal dilatation of the sinuses of Valsalva may distort the relationships of the cusps and contribute to insufficiency in this way Syphilitic aortic insufficiency may be asymptomatic for many years but with the onset of congestive failure the mortality rate rises precipitously Unless death supervenes from some other cause congestive failure almost invariably develops As with other forms of cardiovascular syphilis there is a high incidence of neurosyphilis in these patients approximately 25% of patients suffering from cardiovascular syphilis will have demonstrable neurosyphilis Rupture of valve cusps occasionally occurs but more often the signs of aortic insufficiency may be due to retroversion of a cusp particularly the right anterior aortic cusp

Significant aortic insufficiency is frequently associated with sensations of pounding or throbbing in the head and neck and with awareness of increased forcefulness of the cardiac thrust even when cardiac compensation is maintained Dyspnea on exertion is usually the first symptom of impending failure Angina pectoris as a consequence of coronary ostial stenosis occurs frequently The presence of coronary pain is not particularly helpful in differentiating syphilitic aortic insufficiency from that due to rheumatic heart disease since it does occur in both especially after the onset of congestive failure Angina is probably more common in syphilitic than in rheumatic aortic insufficiency

Physical examination reveals enlargement of the heart to the left with displacement of the cardiac apex down and outward A blowing high pitched diastolic murmur of low intensity is usually heard best in the second right interspace Often it is transmitted to the left of the sternum where it is heard in the third and fourth interspaces at the parasternal line An aortic systolic murmur may be heard but its presence does not necessarily signify the presence of aortic stenosis An Austin Flint murmur is present in some patients This presystolic apical murmur must not be confused with the murmur of mitral stenosis although differentiation by auscultation alone is sometimes difficult As a general rule when the Austin Flint murmur is present there will not be accentuation of the mitral first sound an opening snap of the mitral valve or accentuation of the pulmonic second sound all of which are common in mitral stenosis Peripheral signs of aortic insufficiency primarily those of a widened pulse pressure and of a low diastolic pressure will be found Occasionally instead of the soft blowing diastolic murmur a rather loud musical aortic diastolic murmur may be heard This is sometimes due to rupture of an aortic cusp or more frequently is the result of retroversion of one of the valve cusps it is not common

Radiographic examination is of help in that it may demonstrate left ventricular enlargement or calcification of the ascending aorta fluoroscopic examination is also of value in delineating both size and overactivity of the left ventricle

Difficulty sometimes arises in attempting to differentiate syphilitic aortic insufficiency from that due to rheumatic fever A positive sero

logic test alone is not necessarily enough to establish the diagnosis Dynamic aortic stenosis with some insufficiency is likely to be rheumatic rather than syphilitic in origin Because of the nature of the pathologic process, aortic stenosis does not occur as a consequence of syphilitic aortitis The fact that calcific aortic valvular lesions have been demonstrated in some patients with proved cardiovascular syphilis does not mean that syphilis was the causative agent The presence of a mitral valvular lesion detected on physical examination and by radiographic means with demonstration of enlargement of the left atrium or calcium in the mitral valve is evidence against the possibility of an associated aortic valvular lesion being syphilitic in origin Atrial fibrillation is distinctly uncommon in cardiovascular syphilis Its presence would lead one to suspect that the disease was rheumatic rather than syphilitic

CORONARY OSTIAL STENOSIS

Coronary ostial stenosis is a complication in slightly less than one fourth of the patients with syphilitic aortitis Although it occurs as an isolated manifestation, usually it is associated with aortic valvular disease and aortic insufficiency Narrowing or complete occlusion of one or both coronary ostia may occur as a result of fibrous thickening and hyalinization of the intima near the coronary ostia as well as by scarring of the media The arteritis rarely involves the coronary arteries themselves. Myocardial infarction as a result of ostial stenosis does occur but is uncommon For unexplained reasons, isolated coronary ostial stenosis is often asymptomatic and not necessarily associated with the effort pain seen in coronary atherosclerosis Sudden death does occur in this group of patients If symptoms of coronary insufficiency are present, aortic insufficiency is likely to be present as well Paroxysmal substernal pain not related to exertion, sometimes with radiation to the back has been described The presence of anginal pain in the patient with a positive serologic test for syphilis does not make an unequivocal diagnosis of coronary ostial stenosis, even if aortic insufficiency is present In any patient with cardiovascular syphilis, one must keep in mind that coronary atherosclerosis may also be present and may be the cause of the anginal pain Coronary ostial stenosis may lead to rapidly progressive congestive failure and may be as important a factor as the presence of the aortic valvular lesion itself

SYPHILITIC ANEURYSMS

Although fusiform aneurysms in the form of limited and localized dilatations of the aorta do occur, saccular aneurysms, either single or multiple, are far more common Saccular aneurysms occur with greatest frequency in the ascending aorta and in the arch In a sense, a gradient exists from the proximal to the distal aorta Aneurysms are less frequent in the descending thoracic aorta A few are seen in the upper abdominal aorta above the origin of the renal artery, but below the renal arteries they are extremely rare. Aortic aneurysms vary greatly in size Their clinical manifestations depend upon their location and upon the structures which they compress or displace Aneurysms of the ascending aorta have been referred to in the older literature as "aneurysms of signs" whereas aneurysms of the arch of the aorta have been called "aneurysms of symptoms" because of the way in which they interfere with structures in that area Less common than aortic aneurysms are aneurysms of the sinuses of Valsalva. These relatively small aneurysms tend to dissect into the membranous portion of the interventricular septum and as a rule produce few or no symptoms unless rupture of the aneurysm occurs Syphilitic aneurysms of the innominate artery are occasionally seen (Fig 3) Aortic aneurysms must be differentiated from mediastinal tumors Radiographically, aneurysms appear as dense rounded masses with smooth borders which are contiguous with the aorta Fluoroscopic examination may reveal expansile pulsations in some but not in all instances Pulsations are absent if the aneurysmal sac has been obliterated by the deposition of many layers of thrombus Occasionally differentiation from mediastinal tumors can be made only by angiocardiography which will



Fig 3 A syphilitic aneurysm of the innominate artery in a 50 year old man He complained of pain and swelling in the neck and of a chronic nonproductive cough A pulsating tumor was present in the neck

outline the vascular structures The aneurysmal sac is not always delineated by the contrast medium because of the presence of a thrombus within the sac

Aneurysms of the sinuses of Valsalva may develop in any of the sinuses They do not produce symptoms except in a few rare instances in which they cause functional stenosis of a valve usually either the pulmonic or the tricuspid valve as a result of compression of the valve ring As the aneurysm enlarges it can bulge into either atrium or either ventricle Rupture can occur into any of these chambers but most frequently into the right atrium or right ventricle Rupture is usually accompanied by pain and dyspnea The physical signs are those of a murmur resembling that of a patent ductus this is best heard over the upper portion of the sternum Intractable right heart failure is the common sequel to rupture of such an aneurysm and life expectancy is limited

Aneurysms of the ascending aorta tend to lie anterior and lateral to the aorta As they increase in size erosion of the ribs to the right of the sternum may take place (Figs 4 and 5) This is associated with relatively severe bone pain If the aneurysm is sufficiently large pulsations may be felt in the second and third intercostal spaces The trachea is often displaced to the left The aneurysm may also obstruct the right ventricular outflow because of compression of the pulmonary artery and may in this way precipitate right heart failure Aneurysms of the ascending aorta may compress the major bronchi and have been reported to produce partial superior vena caval obstruction Aneurysms of the ascending aorta may rupture into the pulmonary artery This catastrophe is usually attended by severe pain intense dyspnea and signs of peripheral vascular collapse The physical signs are those of an arterial venous shunt including systolic and diastolic murmurs over the upper portion of the sternum and a widened pulse pressure If death does not occur immediately signs of right heart failure ultimately develop The murmur in the case of rupture into the pulmonary artery does

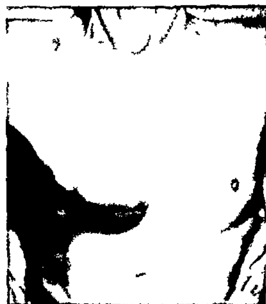


Fig 4 Syphilitic aneurysm of the aorta in a 65 year old man which has eroded through the right anterior chest wall This patient's chest films are shown in Figure 5



Fig 5 Two syphilitic aneurysms of the aorta in the patient shown in Figure 4 The lateral film demonstrates the extensive calcification of the ascending aorta Calcification of the aortic annulus is also seen

not closely simulate that of a patent ductus arteriosus the systolic murmur is as a rule more prominent than the diastolic murmur which tends to be of relatively short duration If an aneurysm ruptures into the superior vena cava the auscultatory signs of a typical arterial venous fistula appear and in addition an elevation of venous pressure occurs *in the upper half of the body Cyanosis probably* as a result of venous stasis has been reported Aneurysms of the ascending aorta may on occasion rupture into the pericardium with the rapid production of fatal cardiac tamponade or they may rupture into a bronchus

Syphilitic aneurysms of the arch of the aorta are more prone to be associated with symptoms fairly early because of the close relationship of the aorta at this point to the esophagus trachea recurrent laryngeal and phrenic nerves and vertebral bodies Com*pression of the esophagus* produces dysphagia Pressure upon either the trachea or the left main stem bronchus may be responsible for cough Further compression of the left main stem bronchus can eventually lead to atelectasis of part of the left lung The left recurrent laryngeal nerve is not infrequently involved and as a consequence hoarseness and dysphonia may develop Paralysis of the left leaf of the diaphragm may occur as a result of involvement of the left phrenic nerve by *the aneurysm Horner s syndrome is occa*sionally seen Aneurysms in this location may also produce superior vena caval obstruction Stridor is not uncommon Continued pressure upon and pulsation against the thoracic vertebrae produce erosion of the vertebral bodies particularly those of the fourth fifth and sixth vertebrae This is associated with rather severe pain and indeed pain from this source may be the presenting symptom Physical signs are not always prominent but pulsations may be detected in the suprasternal notch Sometimes a tracheal tug can be elicited

Aneurysms located in the descending thoracic aorta produce few symptoms The most

common one is that of bone pain as the result of erosion of the vertebral bodies If the erosion is sufficiently severe nerve root compression or signs due to actual spinal cord compression occasionally occur

TREATMENT OF CARDIOVASCULAR SYPHILIS

Treatment of cardiovascular syphilis as well as syphilis generally has been simplified considerably since the advent of penicillin in 1944 At the present time there is little indication for the use of the arsenicals in treatment In the uncomplicated case of cardiovascular syphilis treatment either with bismuth or with iodides before a course of penicillin is probably unnecessary since the incidence of serious reactions to penicillin is very low Occasional Herxheimer reactions will occur In rare instances a therapeutic paradox may develop in which the patient s cardiovascular status worsens following treatment This is the result of rapid healing of the syphilitic lesions by scarring near the coronary ostia with further decrease in size of the ostia A minimal course of penicillin consists of 600 000 units of the aqueous procaine preparation daily for two weeks

Symptomatic treatment of angina pectoris or of congestive failure is indicated whenever these conditions are present Older methods which have been advocated for the treatment of syphilitic aneurysms such as wrapping with cellophane or wiring the aneurysm to promote the deposition of a thrombus within the sac are of relatively little value When the aneurysm is saccular with a relatively narrow base it is sometimes possible to excise the aneurysm In selected cases aortic prostheses may be used

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CHAPTER 32

Cardiac Arrhythmias

Ernest O Theilen M D

Disturbances of the cardiac rhythm are relatively common and of sufficient clinical importance to require accuracy and care in their diagnosis and treatment Some of the rhythm disturbances which are not associated with organic heart disease are unfortunately mistaken for manifestations of cardiac damage by physicians and by heart conscious patients resulting in needless anxiety and even invalidism The importance of the recognition of these benign arrhythmias and their interpretation to the patient as a nuisance is as important in many respects as the diagnosis and treatment of more serious mechanism disturbances Precision in the diagnosis of those arrhythmias which may be threatening to life itself is mandatory for the selection of proper treatment since error in judgment may well have disastrous results At times the treatment of a cardiac arrhythmia will present itself as an emergency and under these circumstances electrocardiographic verification may not always be possible Physicians should not become so dependent upon this helpful laboratory procedure that they abandon the examination of the patient Proper diagnosis can be made on the basis of clinical study alone in many cases

From a physiological standpoint the deleterious effects of some arrhythmias are readily understandable because of the way in which they may alter the mechanical efficiency of the heart either in terms of the cardiac output or in terms of the energy expenditure of the myocardium and its efficiency in the performance of a given amount of work Increases in heart rate may lead to relative coronary insufficiency The altered hemodynamics produced by a cardiac arrhythmia may therefore produce the varied symptoms of angina pectoris cardiac failure or the Adams Stokes syndrome

Knowledge of some of the properties of cardiac tissue is necessary for an understanding of the disturbances which may occur in cardiac impulse formation and conduction The most important of these are (1) automaticity (2) conductivity and (3) excitability It is the nodal tissue which specifically possesses the property of automaticity or of rhythmic impulse formation The centers composed of nodal tissue and often referred to as pacemakers may in a sense be considered as miniature oscillators Whether their rythmic discharge is the result of recurring chemical processes or of electrical phenomena or both is debatable Some cardiac physiologists believe that acetylcholine is intimately related to impulse formation One should keep in mind that the electrical activity of the pacemaker itself cannot be detected in the electrocardiogram and the rate of discharge of the pacemaker as well as its location can only be inferred from the minute electrical currents which are produced in the conduction of this impulse through the myocardium A definite gradient of activity exists between the pacemakers of the heart the slower pacemakers being dominated by those with the inherently more rapid rates of impulse formation As a rule the rate of discharge from the sino atrial node is somewhat greater than that from the atrio ventricular node and the intrinsic rate of the A V node is in turn more rapid than that of an idioventricular pacemaker lying in the conducting system below it The cardiac pacemakers and the sino atrial node in particular may also be influenced by external stimuli either of neural or humoral origin

Cardiac tissue in a normal metabolic state and following recovery from any previous depolarization has the property of being able to conduct the stimulus produced by the discharge of a cardiac pacemaker. The speed of conductivity varies, being slowest in the nodal tissue and fastest in the Purkinje network. Normally the impulse generated in the S-A node is conducted in a radial fashion and with a uniform wave front through the atrial musculature to the A-V node, whence it is conducted through the branches of the bundle of His, the Purkinje system, and finally to the *myocardial fibers. There is reason to believe* that depolarization of the interventricular septum begins near the lower or distal end on the left side and that the wave of activation then passes from left to right as well as in a retrograde fashion to activate the muscle fibers of the septum itself. Probably only a small portion of the interventricular septum is activated by impulses passing down the right branch of the bundle of His.

After excitation, cardiac tissue passes through a recovery phase ordinarily referred to as the refractory period. During this time when repolarization occurs, impulses which reach such tissue are without effect and do not result in depolarization of the tissue in question. Variations in the refractory state do exist, and under certain circumstances the refractory phase may be incomplete, resulting in abnormalities of conduction. The dissociation which may occur when impulses arising from a pacemaker fail to stimulate tissue in the refractory phase of its normal cycle must be differentiated from block. The failure of conduction of an impulse in heart block is the result of an abnormally prolonged refractory phase. The significance of the interrelationship of these properties of cardiac muscle will be brought out in the discussion of the individual arrhythmias.

Classification of Arrhythmias

1. *Normal Rhythms*
   - Normal sinus rhythm
   - Sinus tachycardia
   - Sinus bradycardia
   - Sinus arrhythmia
2. Sinus Arrest and Sino-atrial Block
3. Atrial Arrhythmias
   - Atrial premature beats
   - Paroxysmal atrial tachycardia
   - Atrial flutter
   - Atrial fibrillation
4. Atrio-ventricular Nodal Arrhythmias
   - Wandering pacemaker
   - Nodal rhythm
   - Nodal premature beats
   - Nodal tachycardia
5. Atrio-ventricular Heart Block
6. Wolff-Parkinson-White (WPW) Mechanism
7. Ectopic Rhythms of Ventricular Origin
   - *Ventricular premature beats*
   - Idioventricular rhythm
   - Ventricular tachycardia
   - Ventricular fibrillation

NORMAL RHYTHMS

NORMAL SINUS RHYTHM

When the heart beat is initiated and controlled by impulses arising within the sino-atrial node, the cardiac mechanism is called a sinus rhythm. The heart rate in a person with a normal sinus rhythm may vary within rather wide limits. The average resting rate for adult men is 70 to 75 beats per minute and that of women slightly higher. The heart rates of young children at rest are higher than those of the adult, and in the new-born may be as fast as 150 beats per minute. There is a gradual decrease in resting heart rates of children until approximately the age of 6 years, when the heart rate approaches that of the adult. Sinus rhythms can be modified by external influences such as those mediated through pressure and chemical receptors in the carotid sinus and the aorta, by central nervous system influences, and by humoral mechanisms.

SINUS TACHYCARDIA

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SINUS TACHYCARDIA

The division between a normal sinus rhythm and either a sinus tachycardia or a sinus

bradycardia is arbitrary, a sinus tachycardia in adults is defined as impulse formation originating in the S A node, occurring at rates of 100 per minute or more, and followed by normal atrio-ventricular conduction In sinus tachycardia, the rate may be as high as 180 beats per minute, but this is usual only with extreme physical exertion Sinus tachycardia is a normal response to physical exertion and to emotions such as fear, anger, or anxiety It is a compensatory mechanism in hypotension following hemorrhage and in decreased peripheral resistance as a result of vasodilation produced by drugs, external heat or fever. Caffeine, nicotine, and sympathomimetic drugs also tend to accelerate the heart An increase in the metabolic rate as in thyrotoxicosis is commonly associated with a sinus tachycardia Sinus tachycardia may be associated with systemic infections as well as those inflammatory processes confined to the myocardium or pericardium It is one of the manifestations of cardiac failure

The differentiation of sinus tachycardia from other tachycardias as a rule presents no difficulty Occasionally at very rapid rates, the differentiation of sinus tachycardia from paroxysmal atrial tachycardia becomes of some importance Sinus tachycardia differs from paroxysmal atrial tachycardia in that clinically there tends to be some variation in heart rate which can often be influenced by vagal stimulation such as carotid sinus massage In contrast to the slowing produced in sinus tachycardia, carotid sinus massage either has no effect or abruptly terminates a paroxysmal atrial tachycardia The electrocardiogram is also helpful in differentiation inasmuch as normal P waves with normal P R intervals can be identified in sinus tachycardia, but in paroxysmal atrial tachycardia the P waves appear to arise in an ectopic focus

As a rule, treatment need not be directed toward the sinus tachycardia itself but should be aimed at correction of the predisposing factors and any underlying disease

SINUS BRADYCARDIA

Sinus bradycardia is said to exist when the rate of discharge from the S-A node is less than 60 per minute Sinus bradycardia may occur in perfectly normal hearts, it is common during sleep, and may be present in trained athletes during waking hours as well It may be the result of increased carotid sinus sensitivity or of vagal stimulation of other origin as in vaso-vagal syncope Increased intracranial pressure is associated with a decrease in heart rate High serum concentrations of bile salts appear to exert a depressive action on the myocardium and are associated with sinus bradycardia Starvation, myxedema, or other states with reduced rates of metabolism may be accompanied by bradycardia Treatment for the bradycardia itself is seldom necessary

SINUS ARRHYTHMIA

The term sinus arrhythmia is used to describe a regularly recurring variation in the rate of impulse formation at the sinus node consisting of periods of gradual slowing and acceleration Sinus arrhythmia often, but not invariably is related to the phases of the respiratory cycle, characteristically the pulse rate tends to increase during inspiration and to decrease with expiration It can often be abolished by breath holding and becomes much less apparent during increases in heart rate associated with physical exertion This normal variation of a sinus rhythm is very common in children and tends to become less evident in adults When a sinus arrhythmia is associated with marked changes in heart rate it may be mistaken for other arrhythmias such as atrial fibrillation Clinical differentiation can be made if one keeps in mind the fact that there is a recurring pattern in sinus arrhythmia, and that the arrhythmia can be temporarily abolished by breath holding as well as by exercise In rare instances, sinus arrhythmia may be confused with sino atrial block, second degree A-V heart block, blocked atrial premature beats, and wandering pacemakers Sinus arrhythmia is immediately identifiable on the EKG tracing by the presence of normal P waves and normal A-V conduction times Reassurance of the patient is the only therapy required

SINUS ARREST AND SINO-ATRIAL BLOCK

Sinus arrest and sino atrial block although similar in their clinical manifestations differ in mechanism The former is associated with cessation of activity or failure of impulse formation in the sino atrial node while in the latter impulse formation in the S A node continues in a normal fashion but the impulse is not conducted from the node through the atrial muscle As a consequence of either of these arrhythmias asystole may occur As a rule this is transient since the subsidiary pacemakers will assume control of the heart rhythm or a normal rhythm is promptly resumed Occasionally however prolonged asystole will occur leading to syncope Ventricular standstill may terminate in death Sinus arrest may be the result of carotid sinus hypersensitivity may occur during anesthesia and surgery and may follow medication with drugs such as quinidine Sino atrial block also may be induced by carotid sinus stimulation quinidine digitalis and hyperpotassemia

Sinus arrest cannot be diagnosed by clinical examination Sometimes it can be excluded if inspection of the jugular pulse reveals the presence of definite "a" waves resulting from atrial contraction Inspection of the electrocardiogram will reveal no atrial activity in the case of sinus arrest In sino atrial block the longer R R intervals produced by intermittent S A block will be more or less precise multiples of the basic R R intervals

When sinus arrest is the result of carotid sinus hypersensitivity atropine in doses of 0 3 to 0 6 mg three times a day may be tried in an attempt to suppress excessive vagal stimulation However various sympathomimetic drugs are more effective in the management of these problems These include ephedrine, 15 to 30 mg by mouth three to four times daily hydroxyamphetamine hydrobromide (Paredrine) 20 to 60 mg three to four times daily and isoproterenol hydrochloride (Isuprel) 5 to 15 mg sublingually four times a day Ventricular standstill following prolonged sinus arrest requires immediate treatment as soon as it becomes evident Stimulation of the heart by striking the chest wall over the precordium is often effective in initiating contractions This also can be accomplished by pricking the surface of the heart with a long small bore needle or by intracardiac injection of dilute epinephrine Recently an external electrical stimulator or pacemaker has been shown to produce effective ventricular contractions and an effective cardiac output If cardiac arrest occurs during anesthesia or surgery an immediate thoracotomy and cardiac message may be life saving If massage alone does not restore ventricular contractions it may be necessary to try intracardiac injections of dilute epinephrine or calcium chloride solution as well

ATRIAL ARRHYTHMIAS

ATRIAL PREMATURE BEATS

The normal intervals in a cardiac rhythm may be disturbed by impulses which occur early in the cycle and which because of premature depolarization and interference with the normal pacemaker are followed by periods of cardiac inactivity greater than the normal cycle length The old term "extrasystole" cannot properly be applied to this phenomenon True extra systoles do occur they may also be called interpolated beats In this situation the ectopic beat falls midway between two normal beats and is not followed by a compensatory pause Most supraventricular premature beats arise in ectopic foci and not in the normal pacemakers They are called atrial premature beats Premature beats of S A nodal origin occur infrequently they can be distinguished from atrial premature beats by differences in the P waves in the sinus and in the ectopic beats Premature beats may occur either singly or in short runs Most atrial premature beats are of no clinical significance but they do occur with increased frequency in patients with rheumatic heart disease and valvular damage particularly mitral

stenosis or insufficiency, in coronary artery disease and after myocardial infarction Digitalis toxicity is more likely to be associated with ventricular premature beats but occasionally the atrial variety is seen as well Emotional disturbances and such relatively innocuous stimuli as coffee and tobacco may precipitate them

The precise mechanism responsible for the occurrence of premature beats is not known Several theories have been advanced including (1) intermittent discharge of a normally inactive ectopic focus, (2) re-entry of an impulse generated in a normal pacemaker into tissue not depolarized initially by the impulse and (3) discharge of a parasystolic pacemaker All three of these mechanisms are possibly operative in different situations Discharge from a normally inactive ectopic focus would not be expected to show any particular relationship either to the preceding normally conducted impulses or to each other In a very large number of premature beats of either atrial or ventricular origin there appears to be a fairly definite relationship between at least the first premature beat of a group, if they are multiple, and the preceding normal complex The fixed time interval which may occur between these two beats (the normal and the ectopic) tends to support the re-entry theory This theory presupposes that during normal depolarization some tissue remains refractory and that as a result the activating impulse passes around it only to return to it at a somewhat later time by a somewhat circuitous route It would then be possible for the impulse to continue to pass through the muscle in a circuitous route perpetuating the ectopic rhythm This mechanism could apply in either atrial or in ventricular premature beats

The theory of a parasystolic focus assumes the existence of an ectopic pacemaker within the muscle which is in some way protected from sinus impulses so that the ectopic pacemaker is not discharged by the normal sinus impulses The ectopic pacemaker may manifest itself in regularly recurring beats occurring at multiples of a basic time interval, ordinarily, these ectopic beats do not occur in a perfectly regular manner because some of the impulses generated in the ectopic pacemaker are presumably blocked. Parasystolic premature beats also differ from the more common type thought to be due to re-entry in that coupling to the preceding normal QRS complex is not fixed but is often quite variable

Atrial premature beats as a rule are asymptomatic, but at times patients complain of palpitation or of sensations analogous to "skipping," "flopping" or of the heart "turning over" Atrial premature beats, especially when numerous may be premonitory signs of paroxysmal atrial tachycardia or of atrial fibrillation From a clinical standpoint, the effort to distinguish between atrial, nodal, and ventricular premature beats is not very rewarding Auscultation of the heart will reveal a quick beat followed by a compensatory pause, the contraction following this pause is more forceful than either of the preceding beats because of the prolonged diastolic filling time Occasionally the occurrence of premature beats cannot be detected on palpation of the pulse and only a prolonged interval suggesting a dropped beat will be noticed This occurs because the premature beat may occur so early that ventricular filling cannot be accomplished and as a consequence the stroke volume may not be sufficient to produce a palpable pulsation

The electrocardiographic diagnosis of atrial premature beats is made when an abnormal P wave occurs early in the normal cycle and is followed after an interval of 0 12 seconds or more by a QRS complex not appreciably different from those of the normal cycle The premature complex is followed by a compensatory pause, and resumption of activity of the normal pacemaker

Occasionally the premature atrial impulse is not conducted through the A-V node and blocked premature beats occur If the premature atrial impulse occurs when the conduction system below and including the A V junctional tissue has not fully recovered and while some areas are still in a relatively refractory phase, the associated QRS complex may be distorted in contour and prolonged in time resembling a complex from an ectopic ventricular focus This is called aberrant ventricular conduction and is distinguished

as such and differentiated from a ventricular ectopic beat by its association with an ectopic P wave

Treatment is not often required but in a patient with organic heart disease in whom the possibility of a more serious rhythm disturbance arises digitalization may be considered Quinidine in a dose of 0 2 to 0 4 gm three to four times a day is also effective in the control of atrial premature beats but the response in a given case is not always predictable Quinidine should be avoided when cardiac failure is present or when the atrial premature beats are the result of digitalis intoxication When digitalis intoxication is present the oral administration of potassium chloride is the best form of treatment If undue gastric irritation is encountered use of the enteric coated preparation usually will prevent such difficulty An approximate dose of 2 gm three times a day is used until evidence of digitalis toxicity has disappeared The possibility of potassium intoxication always must be kept in mind

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA (Atrial and Nodal)

Paroxysmal supraventricular tachycardias may originate either in an ectopic atrial focus or in the A V nodal tissue Because of their similar clinical manifestations and treatment they will be considered together Differentiation of one form from the other is not always possible even by electrocardiography These tachycardias are essentially a rapid succession of premature beats without the usual compensatory pauses In the following discussion many of the remarks concerning paroxysmal atrial tachycardia (PAT) are applicable to nodal tachycardia as well

Paroxysmal supraventricular tachycardia occurs in patients without other evidence of heart disease but it may be associated with such disorders as acute infections acute rheumatic fever thyrotoxicosis and coronary artery disease or myocardial infarction It may occur intermittently in patients exhibiting the Wolff Parkinson White mechanism Over indulgence in alcohol or tobacco and gastrointestinal disturbances have been implicated These tachycardias may precipitate attacks of angina pectoris in patients with coronary artery disease Paroxysms of atrial tachycardia are not benign in children and may result in cardiac failure and death Palpitation is the main symptom but the reduced cardiac output may lead to associated weakness dizziness or syncope Dyspnea and other manifestations of cardiac failure may develop

The heart rate in paroxysmal tachycardia varies from 150 to 250 beats per minute and the rhythm is perfectly regular Carotid sinus massage either will have no effect or will terminate the arrhythmia suddenly sometimes within the space of one beat while it generally only slows a sinus tachycardia Furthermore the paroxysms of tachycardia begin abruptly again within the space of one beat instead of by a gradual increase in rate The heart sounds in PAT are monotonously constant in loudness In uncomplicated paroxysmal atrial tachycardia neither the first nor the second heart sound is widely split as is often true in a ventricular tachycardia However the supraventricular tachycardias (atrial or nodal) may occur with functional bundle branch block or aberrant conduction in which case asynchronous contraction of the ventricles may produce wide splitting of the heart sounds particularly of the first heart sound Ordinarily there is no variation in loudness of the first sound and on examination of the venous pulse in the neck no irregular "a" waves will be seen When the tachycardia originates in the A V node variations in loudness of the first sound occur if there is retrograde block of the nodal impulses This produces A V dissociation and as a result of the independent atrial activity right atrial contraction may be superimposed on right ventricular contraction producing large "a" waves or Cannon waves in the veins of the neck This is a rather uncommon situation

The electrocardiogram in paroxysmal atrial tachycardia (Fig 1) exhibits P waves of ectopic origin In paroxysmal nodal tachycardia the P waves may be retrograde occurring before or after the QRS complex or no P



Fig 1 Lead II Paroxysmal atrial tachycardia at a rate of 187 per minute showing abrupt spontaneous termination of the tachycardia An atrial premature beat is evident following conversion of the tachycardia This 12 year old girl had no demonstrable heart disease

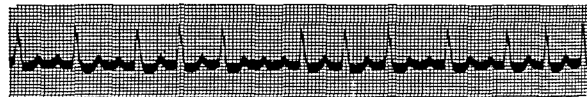


Fig 2 Lead II Paroxysmal atrial tachycardia with variable A V block in a 70 year old man The atrial rate is 284 per minute

waves may be seen at all in a mid nodal focus The QRS complex very closely resembles that seen during normal sinus rhythm unless aberrant ventricular conduction is present These arrhythmias differ from sinus tachycardia in which the P waves are of normal contour Atrial flutter particularly when it occurs with 2 1 block may need to be considered in the differential diagnosis The effect of carotid sinus *pressure may be very* helpful in the differential diagnosis in doubtful cases Paroxysmal atrial tachycardia will respond with abrupt termination or not at all *Transient slowing* occurs in sinus tachycardia but with atrial flutter the block may be temporarily increased and during these periods the flutter waves are seen clearly on the electrocardiogram

An interesting type of paroxysmal atrial tachycardia usually associated with some degree of A V block is seen as a manifestation of digitalis intoxication Certain factors other than excessive amounts of digitalis *should be* kept in mind since even properly digitalized patients may develop this arrhythmia as well as other cardiac arrhythmias if there has been *an excessive loss of* potassium Patients who are not eating well or who are receiving energetic diuretic therapy may develop potassium depletion which will tend to accentuate the toxic effects of digitalis The atrial rate in these instances may vary from 150 to 250 beats per minute but unlike the usual paroxysmal atrial tachycardia varying degrees of A V block may be present so that the ventricular response is below that of the atria The ventricular rhythm will be irregular when the A V block is inconstant An isoelectric baseline between the P waves and the presence of digitalis effect in the electrocardiogram may be helpful in differentiating this particular arrhythmia from the usual *paroxysmal atrial tachycardia* (Fig 2)

When paroxysmal atrial tachycardia is the result of digitalis intoxication the administration of potassium is the treatment of choice and is practically specific Potassium chloride may be administered in divided doses usually not exceeding a total of 6 gm in 24 hours If the patient is unable to take oral medication it may be administered by slow intravenous drip Caution is required because of the possibility of potassium intoxication and the drug must be administered slowly to avoid transient rises of blood potassium to *toxic levels*

Vagal stimulation in one of several ways may be sufficient to interrupt the usual paroxysm of atrial tachycardia Carotid sinus massage is the most effective mechanical means of stimulating the vagal mechanism It should be attempted first on the right and later on the left if necessary Massage should never be performed on both sides simultaneously and never for *longer than 30 seconds* Vagal stimulation by pressure on the eyeballs is

at times helpful but is distinctly unpleasant and damage to the eyes is possible Self induced gagging or vomiting is sometimes effective as is ipecac induced vomiting Valsalva maneuvers will occasionally terminate this arrhythmia When these simple measures fail prostigmine methylsulfate should be administered in a dose of 0 5 to 1 0 mg subcutaneously Its effect can be reinforced by carotid sinus massage at the time intestinal cramps appear This drug should not be used in patients with bronchial asthma Mecholyl is an extremely potent parasympathetic stimulant but the side effects outweigh the good ones and its use is not recommended Reflex vagal stimulation by pressor amines such as Neo Synephrine also is effective This drug should not be used in patients with hypertension or organic heart disease Failure of carotid sinus massage prostigmine or pressor amines to restore a normal rhythm is an indication for digitalis or quinidine Digitalis is the drug of choice for the treatment of this arrhythmia in small children or when cardiac failure is present If necessary an intravenous preparation such as desacetyl lanatoside C (Cedilanid D) 0 8 to 1 6 mg for adults may be given The only reservation in the use of digitalis in the treatment of these paroxysmal supraventricular tachycardias is that it should not be administered when there is doubt about the diagnosis It is contraindicated in paroxysmal ventricular tachycardia If the patient is not critically ill quinidine can be administered by mouth often a single dose of 0 6 gm given in conjunction with a sedative will be followed by restoration to a normal sinus rhythm Other dosage schedules as outlined under atrial fibrillation may be necessary Prevention of recurrences can be achieved either by the administration of small doses of quinidine 0 2 gm three to four times a day (or by any higher tolerable dose if necessary) or by a maintenance dose of digitalis after digitalization

ATRIAL FLUTTER

Atrial flutter is characterized by rapid regular contractions of the atria at rates varying from 250 to 350 beats per minute usually associated with a slower ventricular response It is more often than not a manifestation of organic heart disease Although it is less common than atrial fibrillation both arrhythmias may be seen intermittently in a given patient Rheumatic heart disease particularly with mitral valvular involvement coronary artery disease (particularly following myocardial infarction) thyrotoxicosis acute pulmonary infections pulmonary emboli and crush injuries of the chest are common precipitating causes

Several theories have been advanced to explain the origin of atrial flutter Sir Thomas Lewis s theory of a circus movement around the great veins of the atria and the regular production of so called "daughter waves is well known An alternative explanation is that an ectopic focus within the atria gives rise to regular recurring contraction waves passing in a uniform radial wave front from the ectopic site The circus movement theory cannot be accepted without question but on the other hand neither is the single ectopic focus assumption necessarily correct The theory of re entry mentioned briefly in the discussion of atrial premature beats may be applicable here

Symptomatically atrial flutter differs little from tachycardia of other origin and may be manifested only by palpitation It too may induce angina pectoris in susceptible patients and it can lead to heart failure because of the decreased efficiency of the heart as a pump Examination will reveal ventricular rates of approximately 150 to 165 beats per minute There is often a definite ratio between the atrial and ventricular responses and the even ratios such as 2 1 or 4 1 are more common than odd ratios such as 3 1 These ratios may be relatively constant or may vary producing an irregular ventricular rhythm which is difficult to differentiate from atrial fibrillation It is not often possible to make the diagnosis by clinical examination alone but occasionally inspection of the neck veins during simultaneous auscultation of the heart or palpation of the pulse will reveal a difference between the venous pulsations in the neck and the ventricular response thus differentiating it from PAT without block Atrial flutter with a 1 1 ven

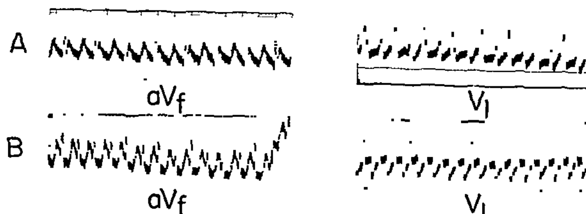


Fig 3 Atrial flutter in a 14 month old infant with a history of numerous episodes of rapid heart action for 3 months Generalized cardiac enlargement was present A Atrial flutter with 2 1 A V block, *the atrial rate is 332 and the ventricular rate 166 per minute* Note the typical flutter waves in aV_f In V1 the saw-tooth pattern is lost, the waves are separate and distinct Every second wave is fused with the QRS B Atrial flutter with a 1 1 response This tracing was taken the following day *Both atrial and ventricular rates are 314 per minute*

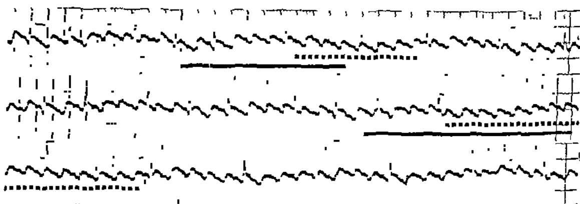


Fig 4 Atrial flutter A continuous strip of lead II showing the effect of carotid sinus pressure in increasing A-V block The solid line indicates the duration of carotid sinus massage The dotted line indicates the period of increased A-V block

ticular response is uncommon and its practical recognition is an electrocardiographic problem (Fig 3) Carotid sinus stimulation will not interrupt atrial flutter but it may produce temporary ventricular slowing, often in step-wise fashion (Fig 4)

The electrocardiographic diagnosis is made from the presence of regularly recurring flutter waves *resembling in certain respects a sine* wave Ventricular responses will occur either in a fixed or a variable ratio to these flutter waves Precordial leads, particularly V1 and V2 may not show the typical "saw tooth" flutter waves *because atrial complexes are more distinct in these leads* and in esophageal leads at atrial levels In those leads demonstrating typical flutter waves, the negative component of the wave probably represents repolarization of the atrium and is analogous to the T wave of the QRS complex

Treatment consists of digitalization either by the oral or if necessary by the intravenous *route Digitalis alone may convert the* arrhythmia to atrial fibrillation, and upon withdrawal, reversion to a normal sinus rhythm sometimes occurs Prediction of the course of events is not possible and restoration of a sinus rhythm does not necessarily require that digitalis be stopped Some patients with atrial flutter are relatively refractory to digitalis and require considerably more than the usual digitalizing dose to slow the

ventricular rate Such patients should be observed carefully for evidence of digitalis toxicity Quinidine or pronestyl should not be given to patients with atrial flutter who have not been digitalized Quinidine tends to suppress the rate of discharge from an ectopic focus and slows down conduction through the atrium This action permitting a longer recovery time together with slightly accelerated conduction through the A V node makes possible a 1:1 atrial ventricular response Digitalis will increase delay in conduction at the A V node and this is the reason for digitalizing patients prior to the administration of quinidine When digitalization alone fails quinidine may accomplish conversion of atrial flutter to a normal sinus rhythm When the rate of discharge from the ectopic focus falls below the inherent rate of the S A node which is more resistant to the action of quinidine the normal pacemaker will supercede the ectopic pacemaker Pronestyl is a substitute for quinidine but is somewhat less effective Quinidine is best administered by the oral route 0.2 gm every 2 hours for five doses beginning in the morning of the first day of treatment If conversion to a normal rhythm does not occur the following day the dose is increased to 0.4 gm every 2 hours for five doses If necessary the dose ultimately can be increased step wise to as much as 0.8 gm every 2 hours for five doses if the patient is watched closely for signs of drug intoxication Restoration of a normal sinus rhythm is not always possible but if accomplished prophylactic doses of either quinidine or digitalis are advisable in those patients with a history of recurring paroxysms of flutter Both digitalis and quinidine have been used with success The dose of quinidine is variable but will generally range between 0.2 to 0.4 gm three to four times a day Enteric coated or delayed action preparations may be used to reduce the number of doses per day

ATRIAL FIBRILLATION

Atrial fibrillation is the result of multiple rapid uncoordinated impulses passing through the atrial wall to the A V node producing a totally irregular response of the ventricles This occurs because many impulses arrive at the A V node before it has had a chance to fully recover from the preceding depolarization As in the case of atrial flutter the circus movement theory has not been completely substantiated and other mechanisms may be operative High speed cinematography has shown the presence of very small areas of contraction occurring at rates of 800 to 1 500 per minute as well as coarser wave activity occurring at rates of 400 to 600 per minute The belief has been expressed that atrial fibrillation results from activity of an ectopic atrial focus and that fibrillation occurs when the rate of impulse formation reaches a level at which the atria are incapable of conducting and contracting as a unit

Atrial fibrillation may occur in the absence of organic heart disease but it is one of the more common arrhythmias associated with organic heart disease and is seen in both congenital and acquired forms Atrial septal defects are the most common underlying congenital lesions Rheumatic heart disease particularly involving the mitral valve coronary artery disease myocardial infarction operations within the chest crushing injuries to the chest with myocardial contusion pulmonary embolism thyrotoxicosis and increases in atrial pressures as a result of excessive intravenous fluids or blood are common etiologic factors

Atrial fibrillation is a less efficient mechanism than a normal sinus rhythm primarily because of the excessively rapid ventricular rates which occur in untreated patients and because the irregularity of the ventricular contractions associated with a shortened diastolic interval leads to inadequate ventricular filling The tendency for excessive acceleration on exercise tends to compromise cardiac efficiency further The stroke volume and arterial pressure vary widely under these circumstances

Both the rate change and the irregularity of the heart may be noticed by patients with this arrhythmia but a surprisingly large number are unaware of its presence If the rate is rapid the patient may complain of sensations of "palpitation pounding and skipping" of the heart The old term "delirium cordis"

was most descriptive of this arrhythmia Its onset is commonly associated with the development of cardiac failure Chronic atrial fibrillation predisposes to the formation of thrombi in the atrium and in the auricular appendage, particularly when mitral valve disease is present, and embolic accidents commonly result

Auscultation of the heart *reveals total* irregularity of the ventricular rhythm Long pauses may occur which are not preceded by quick beats This helps to differentiate this arrhythmia from premature beats with compensatory pauses Because of variations in ventricular filling, which is dependent upon the length of the preceding diastolic phase, the intensity of the first sound will vary widely *The stroke volume may at times be negligible* and not all ventricular contractions will be associated with a palpable pulse at the wrist A deficit therefore may exist between the ventricular rate counted at the apex and the wrist Exercise tends to diminish or abolish premature contractions but in atrial fibrillation, the irregular ventricular rhythm is accentuated

In paroxysmal atrial fibrillation, every attempt should be made to restore normal sinus rhythm The indication in chronic atrial fibrillation is not as clear cut, and frequently even if normal rhythm is restored, it reverts to fibrillation within a short time Before restoration is attempted, it is advisable to digitalize patients *with atrial fibrillation to* slow the ventricular rate Digitalis is the most effective drug for treatment, particularly *if there is* associated cardiac failure Patients with thyrotoxicosis and atrial fibrillation are quite resistant to the action of digitalis Digitalis should be administered before quinidine quinidine may convert the fibrillation to flutter with a more rapid ventricular rate If an attempt is made to restore normal rhythm in the digitalized patient, either quinidine or procaine amide may be used, but quinidine is *preferable It is* best administered in daily courses increasing the dose day by day if necessary It is suggested that 0 2 gm be given every 2 hours for five doses the first day, if normal sinus rhythm has not been restored the dose may be increased step wise to 0 4, 0 6, and 0 8 gm every 2 hours for five doses on the second third and fourth days respectively When the higher doses are reached, *careful clinical and electrocardiographic observation* is mandatory to avoid the cardio toxic effects In fact, significant cinchonism is the indication to discontinue the drug before more serious toxic effects appear If pronestyl is used, the initial dose is 0 5 gm every 2 hours for five doses The drug may also eventually be increased to a level of as much as 1 0 gm every 2 hours for five doses Manifestations of toxicity are somewhat similar to those of quinidine Unless fibrillation has been precipitated by some acute insult which can be removed, maintenance on quinidine or pronestyl will be required in *many* cases if heart disease is present, 0 2 to 0 4 gm of quinidine three to four times a day *may be required The enteric coated preparation* of quinidine permits a reduction of individual doses to approximately three per 24 hour period

ATRIO-VENTRICULAR NODAL ARRHYTHMIAS

Wandering Pacemaker

When the site of impulse formation shifts intermittently between the sino-atrial node and the atrio ventricular node the cardiac rhythm *is said to be controlled by* a wandering pacemaker This arrhythmia often discovered only on electrocardiographic examination is a result of intermittent depression of activity in the sino atrial node either by vagal stimuli or occasionally as a result of digitalis A wandering pacemaker is not indicative of organic heart disease It occurs in perfectly normal persons As a result of shifts in the pacemaker, changes in heart rate are seen not unlike those in sinus arrhythmia However, the change in rate with a wandering pacemaker is not associated with the phases of the respiratory cycle Diagnosis of this arrhyth

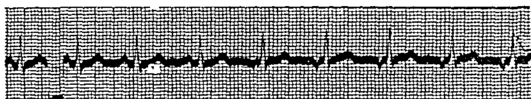


Fig 5 A wandering pacemaker (lead II) in a 39 year old man with no evidence of heart disease

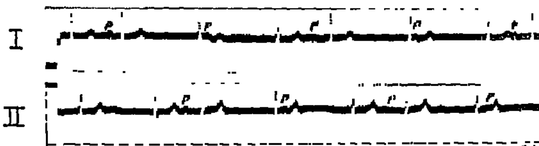


Fig 6 Nodal rhythm with incomplete A V dissociation (interference dissociation) due to retrograde block of the nodal impulses This tracing is from a 74 year old woman with syphilitic heart disease No digitalis The atrial rate is 44 per minute and the basic ventricular rate, 56 per minute In lead I, the second, fifth, and eighth QRS complexes represent ventricular captures by the atrial impulse In lead II, the third and sixth complexes are ventricular captures

mia by physical examination is seldom possible The electrocardiographic diagnosis is made by identification of complexes of normal sinus origin as well as the intermittent complexes originating in the A-V node (Fig 5) In the latter, the P wave will be variable and may show a reversal of polarity because of retrograde conduction The P-R interval will be shorter than 0 12 second, or there may be an R P interval with the P wave following the QRS complex The P wave may also be buried in the QRS complex

A-V Nodal Rhythm

Suppression of S A nodal control usually results in a shift of the pacemaker to the A-V node which then controls both ventricular atrial rhythm This arrhythmia is occasionally seen in persons with normal hearts but it is more often found with organic heart disease As a complication of digitalis therapy it does not necessarily contraindicate continuation of the drug It occurs intermittently during general anesthesia when transient anoxia is probably an important factor Acute infections may precipitate it, and sometimes it is a manifestation of active rheumatic carditis

The heart rate may vary rather widely from 40 to 100 beats per minute In a given situation the heart rate is usually quite constant, and on the basis of physical examination and auscultatory findings it cannot be differentiated clearly from a normal sinus rhythm unless A V dissociation exists A V dissociation occurs in nodal rhythm when the nodal pacemaker is slightly more rapid than the sinus pacemaker and when there is a block of retrograde conduction from the A-V node Complete A-V dissociation on this basis is rare, and is always of short duration More common is incomplete A V dissociation, often referred to as interference dissociation Although the nodal pacemaker discharges at a more rapid rate than the sinus pacemaker and dominates the rhythm occasional sinus impulses reaching the A V node when it is not refractory will lead to isolated ventricular responses which may be mistaken for ectopic beats (Fig 6) Examination of the neck veins may reveal occasional giant "a" waves or Canon waves produced by atrial contraction against the closed tricuspid valve Auscultation will also reveal variations in the intensity of the first heart sound because of the dissociation of atrial and ventricular contractions

Reciprocal rhythm is another variation sometimes seen where the A V nodal pacemaker is dominant This arrhythmia results from the re entry of the cardiac impulse into the A V junctional tissue after its retrograde conduction into the atria For this phenomenon to occur there must be a depression of conductivity in the A V junctional tissue which is not equal in all areas A delay in retrograde conduction is also necessary for its occurrence If this set of circumstances is present an impulse conducted from the A V junctional tissue will spread in a retrograde fashion to the atria producing a retrograde P wave The impulse returns to the ventricles through junctional tissue which no longer is refractory and gives rise to a second ventricular complex This arrhythmia is most often produced by digitalis It is identified on the electrocardiogram by the presence of delayed retrograde conduction from the A V node (usually more than 0 20 second) producing a retrograde P wave which is then followed by a second ventricular complex

NODAL PREMATURE BEATS

Nodal premature beats are indistinguishable clinically from atrial premature beats but there are definite electrocardiographic differences Premature beats of nodal origin like atrial premature beats occur in normal as well as diseased hearts They occur as a manifestation of digitalis intoxication They are distinguished electrocardiographically by the presence of a retrograde P wave occurring early in the cardiac cycle and followed by a P R interval of less than 0 12 second The QRS complex is similar to that seen in the basic rhythm A retrograde P wave may follow the QRS complex when the focus is low in the A V node Occasionally no P waves can be seen and in this situation the diagnosis is made by inference since no distortion or abnormality of the QRS complex itself is present Treatment when necessary is the same as that for atrial premature beats

A-V HEART BLOCK

The rate of conduction through various cardiac tissues is slowest through the A V nodal tissue where the rate is approximately 200 mm per second this is in marked contrast to the rapidity of transmission through the Purkinje network at speeds of as much as 4000 mm per second The delay in conduction at the A V node is variable but as a rule does not exceed 0 20 second It serves a useful purpose in permitting the ventricle to receive the blood ejected by the contraction of the atria Admittedly this does not contribute a large fraction of the total stroke volume but it probably is nevertheless significant Under certain conditions the A V conduction time may be prolonged above the accepted limits of normal This implies an abnormal prolongation of the refractory period of the junctional tissue and cannot be considered a normal variation When this delay in conduction does not result in dissociation of atrial and ventricular contractions incomplete heart block is said to be present Various degrees of this conduction abnormality exist

Incomplete A V heart block characterized only by prolongation of the conduction time through the junctional tissue so that the P R interval exceeds 0 20 second is designated as first degree A V heart block First degree A V heart block is occasionally seen in children with congenital heart disease but is more commonly found as a manifestation of carditis particularly in acute rheumatic fever It may occur in association with other acute infections as well as in coronary artery and syphilitic heart disease One of the more potent actions of digitalis is to delay conduction through the A V node and first degree block is seen very commonly in patients receiving this drug Vagal stimulation may produce first degree incomplete heart block as well as more advanced types including complete A V heart block First degree A V heart block cannot be detected clinically it produces no symptoms It requires no treatment except for measures which can be directed at the removal of the underlying cause

Second degree incomplete A V heart block

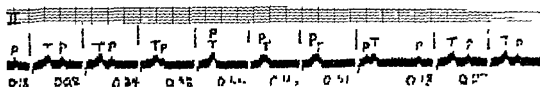


Fig 7 Incomplete A V heart block (Wenckebach type) in a 21 year old man with acute rheumatic fever This tracing shows the gradually increasing delay in transmission of the atrial impulses with ultimate failure of the ventricle to respond

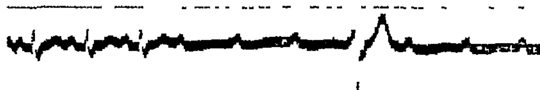


Fig 8 Lead I in a 60 year old man with rheumatic heart disease who had numerous Adams-Stokes attacks This tracing shows sudden complete A V block and ventricular escape

implies that some but not all of the impulses reaching the A V node are transmitted to the ventricle this occasional failure of conduction produces dropped beats A more or less fixed ratio may exist or the block may be variable Second degree heart block can sometimes be detected clinically the presence of one or more dropped beats may be apparent after which the regular rhythm is resumed The pause is not preceded by a quick beat as in the case of premature contractions When a fairly definite ratio such as 2 1 or 3 1 exists the arrhythmia can be suspected if "a" waves are visible in the neck veins and if it is possible to establish the ratio of atrial to ventricular contractions in this way The Wenckebach phenomenon is a form of second degree A V heart block which is characterized by a progressive increase in the A V conduction time of successive beats until eventually complete block of an impulse occurs and a dropped beat follows After the dropped beat A V conduction is again established and the cycle repeats itself (Fig 7) The Wenckebach phenomenon is often produced by digitalis

Complete heart block sometimes designated as third degree A V heart block is a result of failure of any supraventricular impulses to discharge the A V node (Fig 8) Ventricular standstill occurs unless a ventricular pacemaker assumes control with the establishment of an idioventricular rhythm The ventricular rates in these situations will vary from approximately 35 to 40 beats per minute when the idioventricular pacemaker becomes dominant The pacemaker controlling the ventricles may be in the A V junctional tissue rather than below the bifurcation of the conducting system in which case the QRS complexes closely resemble the normal the rate usually will be somewhat more rapid than in the case of an idioventricular pacemaker The same factors responsible for the various forms of incomplete heart block may also be implicated in complete heart block although in the latter the various forms of degenerative heart disease are more common Syncopal episodes in heart block are manifestations either of prolonged ventricular asystole or are the result of a very slow ventricular rate from an idioventricular rhythm which cannot maintain an adequate cardiac output Repeated Adams Stokes attacks may be the result of intermittent complete A V heart block and are likely to occur during those times when the pacemaker shifts from a supraventricular to an idioventricular focus

Asymptomatic complete A V heart block does not require treatment. It may subside spontaneously after recovery from rheumatic carditis diphtheria or myocardial infarction If it is the result of excessive digitalis a normal rhythm will be restored after temporary omis

sion or reduction in dosage of the drug Digitalis is not contraindicated when a patient with complete A-V heart block from other causes develops cardiac failure Patients with complete A V heart block should be cautioned against strenuous physical exertion since this may precipitate syncopal attacks These are the result of the inability of the heart to respond with an increased cardiac output When Adams-Stokes attacks follow ventricular standstill at the onset of an episode of complete block, the measures described under Sinus Arrest should be applied Several sympathomimetic drugs are useful in maintaining an adequate heart rate in complete A V heart block and in preventing recurrent Adams Stokes seizures Epinephrine is an effective drug, but its use generally is restricted to short term therapy When possible it should be given by the subcutaneous or intramuscular routes rather than intravenously Other effective drugs are ephedrine, Paredrine, and Isuprel Isuprel is superior to the other drugs primarily because it is less likely to induce ventricular ectopic beats and ventricular tachycardia or fibrillation It may be given subcutaneously in individual doses of 0 2 mg, by intravenous infusion, or sublingually in doses of 5 15 mg It may be given four times a day, or more often if required *Molar sodium lactate* intravenously is effective in restoring ventricular contractions Initially 10 to 80 ml may be required at one time after which the drug can be given as a slower intravenous infusion, with the rate and the amount dependent upon the ventricular response

THE WOLFF-PARKINSON-WHITE MECHANISM

The Wolff-Parkinson-White mechanism is an abnormality of conduction which involves transmission of impulses from the atria to the ventricles Much of the experimental evidence suggests that in these instances besides conduction through the A V node, there is a secondary pathway which by passes the junctional tissue and because of a more rapid rate of conduction than in the A-V node premature excitation of a portion of the ventricular muscle occurs The Wolff Parkinson-White mechanism has sometimes been referred to as the pre-excitation phenomenon Although this appears to be a developmental abnormality in most cases and is not necessarily associated with any cardiac disease, it does occur in organic disease involving the A V node An alternative explanation for the production of this mechanism disturbance is that accelerated conduction may occur through a portion of the A V node Accelerated conduction could account for premature depolarization of part of the myocardium, with activation of the remaining muscle following transmission of the stimulus through the normal pathway

The Wolff Parkinson-White syndrome is recognized electrocardiographically by a short P-R interval, usually 0 10 second or less, and a prolonged QRS complex The QRS complex is often deformed with slurring of the initial portion of the R-wave The T waves are often inverted in complexes with predominately upright QRS complexes Treatment need not be directed toward abolishing the electrocardiographic abnormality This mechanism is of clinical significance however because many patients with it have paroxysmal supraventricular tachycardias, atrial fibrillation, and atrial flutter Ventricular tachycardia associated with the WPW mechanism is rare Paroxysmal supraventricular tachycardia and atrial fibrillation associated with the WPW mechanism are often misdiagnosed as ventricular tachycardia This confusion results from misinterpretation of the bizarre QRS complexes and from difficulty in identifying P waves in the case of supraventricular tachycardia or the absence of P Waves in atrial fibrillation The usual methods of treatment are applicable when paroxysmal supraventricular tachycardia occurs Paroxysmal atrial fibrillation associated with the WPW mechanism does not respond to digitalization in the usual way The ventricular rate may not slow even though the drug is given to the point of toxicity Although digitalis depresses conduction through the normal pathway it is

thought to have little effect on the anomalous pathway. Occasionally the ventricular rate actually increases after digitalis. Quinidine alone may be effective in restoring a normal rhythm but a combination of digitalis and quinidine is sometimes necessary to terminate the atrial fibrillation.

ECTOPIC RHYTHMS OF VENTRICULAR ORIGIN

VENTRICULAR PREMATURE BEATS

Ventricular premature beats are the most common arrhythmias arising from an ectopic focus and are seen very frequently in normal as well as in diseased hearts. Ventricular premature beats cannot be distinguished clinically from the atrial variety. They are manifested primarily by single or multiple contractions interrupting the basic rhythm and occurring early in the normal diastolic phase. Premature beats may occur at fairly regular intervals together with normal beats, producing combinations such as bigeminal or trigeminal rhythms. A pause longer than the usual diastolic period or R-R interval usually follows a premature ventricular contraction since the first sinus impulse following the preceding normal ventricular depolarization may occur at a time when the tissue is still in the refractory phase from depolarization by the ectopic ventricular beat. On auscultation the sound generated by the premature beat may be less intense than that of a normal beat because of the decreased diastolic filling time, and the heart sounds produced by the first beat following the compensatory pause will be accentuated because of the increased ventricular filling which is permitted by the longer period of diastole. Because the stroke volume produced by ventricular premature beats may be very small, the pulse produced by them may not be palpable at the wrist, and under such circumstances this arrhythmia may be misinterpreted as heart block.

Ventricular premature beats occur in most people at one time or another and as a rule are not indicative of heart disease, especially if they arise from only a single focus. They may be precipitated by fear, anxiety or excitement or may be induced by coffee and tobacco. Various sympathomimetic drugs will also induce them. Ventricular premature beats of multifocal origin are more likely to be associated with heart disease. Ventricular premature beats may be of significance in patients with coronary artery insufficiency and myocardial infarction. One should be suspicious of heart disease if they occur during exercise rather than following exercise. They may be an early manifestation of digitalis toxicity, frequently producing bigeminy.

Patients will often complain of palpitation or pounding of the heart because of the forceful ventricular contractions which follow the compensatory pauses; they may also be disturbed by sensations of "flopping," "turning over," or "skipping" of the heart. Reassurance often is all that is needed in the management of these situations. At times mild sedation may be indicated for patients without organic heart disease. Readjustment of the dose of digitalis is indicated if the premature contractions are the result of digitalis toxicity. When premature beats are the result of digitalis toxicity, potassium salts are specific in abolishing this arrhythmia. Variable amounts of potassium chloride may be necessary; as a rule 4 to 6 gm. will be sufficient; not more than 6 gm. should be given in a 24 hour period. Premature beats often disappear after digitalization in a patient with cardiac failure. Ventricular premature contractions occurring in patients with acute myocardial infarction are ominous in that they may precede bouts of ventricular tachycardia or ventricular fibrillation. Under such circumstances it is advisable to treat this arrhythmia with quinidine in a dose of 0.2 to 0.4 gm. four or more times a day. Pronestyl may also be used in doses of 0.25 to 0.50 gm. four times a day.

The electrocardiographic diagnosis of ventricular premature beats is made whenever

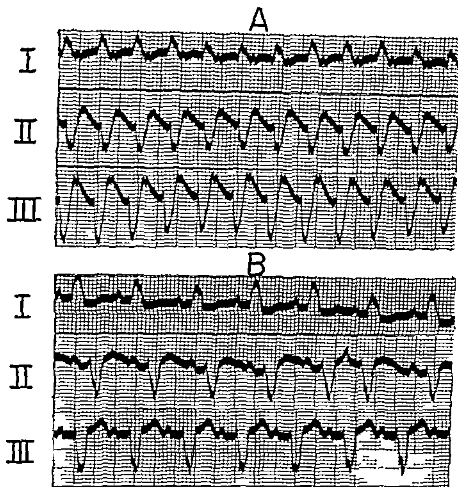
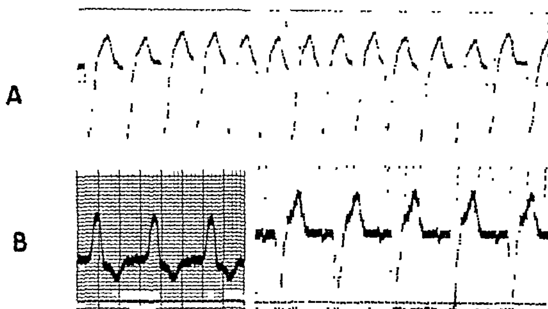


Fig. 9 A This supraventricular tachycardia at a rate of 168 per minute associated with complete left bundle branch block was initially misinterpreted as a ventricular tachycardia Note the deflections in the first portion of the S T segments which represent atrial activity B This tracing taken later in the day confirms the presence of left bundle branch block, complete

wide bizarre QRS complexes appear prematurely in the basic rhythm and are not preceded by ectopic P waves Such QRS complexes are followed by a compensatory pause except in those rare instances in which the premature beat is truly interpolated and occurs between two normal heart beats without disturbing the basic rhythm Such interpolated premature beats are true extrasystoles Ventricular premature beats need to be differentiated from atrial premature beats with aberrant ventricular conduction

IDIOVENTRICULAR RHYTHM

An idioventricular rhythm occurs when, as a result of complete A-V heart block, a pacemaker situated beneath the bifurcation of the A V bundle assumes control of the ventricles This idioventricular pacemaker has an inherently slow rate of impulse formation at approximately 35 to 40 beats per minute In an established idioventricular rhythm, the cardiac output is often adequate for body needs despite the slow rate, but some patients experience shortness of breath and light headedness on exertion because of the inability to increase the cardiac output If the rate slows much below 35 beats per minute, syncopal attacks and the Adams Stokes syndrome discussed elsewhere may occur because of the reduced cardiac output In patients with cardiac rates below 35 beats per minute, various sympathomimetic drugs such



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as ephedrine, hydroxyamphetamine hydrobromide (Paredrine), or isoproterenol (Isuprel) may be used to increase the ventricular rates. The potential dangers of these drugs in inducing ventricular tachycardia or even ventricular fibrillation should be kept in mind.

VENTRICULAR TACHYCARDIA

Ventricular tachycardia is essentially a rapid sequence of ventricular premature beats occurring at rates of 150 to 250 per minute. The mechanism of its production is probably the same as that of isolated ventricular premature beats, and either the theory of re-entry or of parasystole might explain this arrhythmia.

Ventricular tachycardia is seen in patients with coronary artery disease and not uncommonly occurs as a complication of myocardial infarction. It may be the result of digitalis or quinidine intoxication. The symptoms in a patient with ventricular tachycardia are not different than those encountered in the various supraventricular tachycardias, except that here the patient nearly always has significant heart disease.

On physical examination, the heart rate may be perfectly regular or slightly irregular. Consecutive beats do not sound alike primarily because the first sound varies in intensity. The first sound is usually accentuated in comparison with the second heart sound and in fact, the second sound may be inaudible. In those situations in which only one heart sound can be heard in each cycle, the heart rate may be misinterpreted as being one half of its actual value. In other situations the first as well as the second heart sound may be widely split. The variations in intensity of the first heart sound as well as the wide splitting of the first heart sound are helpful in differentiating ventricular tachycardia from most cases of paroxysmal supraventricular tachycardia. When paroxysmal supraventricular tachycardia with bundle branch block is present, the only point of differentiation between this arrhythmia and paroxysmal ventricular tachycardia may be the intensity of variation of the first heart

sound, unless carotid sinus massage produces a change in rate Carotid sinus stimulation has no effect on ventricular tachycardia Paroxysmal ventricular tachycardia is another cause of cardiac syncope

The electrocardiographic diagnosis of ventricular tachycardia is not difficult as a rule Occasionally it may be confused with other arrhythmias such as supraventricular tachycardia with bundle branch block (Fig 9), supraventricular tachycardia with aberrant conduction, and rapid atrial fibrillation with bundle branch block (Fig 10) The demonstration of ectopic P waves in the first two instances and the variations in rate in case of rapid fibrillation are helpful in differentiating these arrhythmias

The presence of a ventricular tachycardia can be considered as an emergency which requires prompt treatment Quinidine or procaine amide are the drugs of choice except when it is due to digitalis intoxication However, neither should be used in paroxysmal ventricular tachycardia occurring in patients with complete heart block Quinidine is administered in a dose of 0 6 to 0 8 gm It may be given safely intravenously if the emergency justifies it and if certain precautions are observed The preparation in the form of quinidine gluconate should be dissolved in a volume of at least 20 cc of saline and injected very slowly over a period of at least 20 minutes during continuous electrocardiographic monitoring and during continuous auscultation of the precordium When a change in rate or rhythm occurs, the injection should be stopped temporarily, and if the tachycardia has converted to a normal mechanism, the entire amount of quinidine should not be given If procaine amide is used, as much as one gram may be given intravenously over a period of 30 minutes Procaine amide will produce significant hypotension in many patients, occasionally severe enough to require the administration of a pressor substance such as norepinephrine (Levophed). After conversion to a normal sinus rhythm, patients may be maintained on quinidine 0 2 to 0 4 gm three to four or more times a day or on procaine amide 0 25 to 1 0 gm four times a day Ventricular tachycardia produced by digitalis intoxication should be treated by the slow intravenous administration of potassium chloride The amount required may vary from 3 to 6 gm or more

VENTRICULAR FIBRILLATION

Ventricular fibrillation, a chaotic uncoordinated and wholly ineffective mechanism for the propulsion of blood as a rule terminates in death A brief paroxysmal form is known to occur, but is uncommon Ventricular fibrillation may follow ventricular tachycardia and is one of the results of intoxication with digitalis or quinidine It may be produced by acute myocardial infarction, myocardial ischemia secondary to coronary artery disease, hypothermia and electric shock

Treatment as a rule is ineffective because it cannot be instituted quickly enough When it occurs during surgical procedures, rapid thoracotomy, cardiac massage, and electrical defibrillation are effective in re-establishing a normal rhythm

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CHAPTER 33

Emotions and the Circulation

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EMOTIONS AND THE CIRCULATION

Somewhere between one third and two thirds of all patients have illnesses that are largely or entirely based on psychophysiological mechanisms[1,2] These disorders may be reflected by the disturbed function of any of the body systems or structures Functional circulatory phenomena are especially common as the cardiovascular system is very sensitively attuned to disturbances in the emotional sphere

PSYCHOPHYSIOLOGICAL CORRELATIONS

An intimate relationship between psychic activity and changes in heart rate has long been recognized[3] The heart rate usually increases with emotion Sinus bradycardia may occur, however either alone or as part of a vasovagal syncopal reaction The tachycardias appear to result from sympathetic overactivity and the sudden release of epinephrine Stimulation of certain areas in the cerebral cortex hypothalamus and brain stem can alter the heart rate as well but the precise role of these higher autonomic centers has still to be fully clarified[4,5] Small amounts of acetylcholine may increase the heart rate but the potential clinical significance here is not clear These tachycardias tend to be transitory and to pursue a recurring but nonprogressive course They are usually abolished by sleep and by sedatives in contrast with those resulting from thyrotoxicosis and other organic processes[3]

Cardiac arrhythmias accompany emotional reactions more often than is generally appreciated[6,7] The abrupt onset of auricular and ventricular premature beats paroxysmal auricular and ventricular tachycardias paroxysmal auricular fibrillation and minor degrees of heart block during psychic stress has been verified both in normal individuals and in patients with cardiovascular disease[8-11] These phenomena have also been deliberately reproduced in such subjects during carefully constructed stress experiments[8,9,11] Most of these arrhythmias (i e those involving SA and AV nodes and the auricles) appear to result from vagal overactivity[12] Excessive sympathetic activity and circulating epinephrine appear largely responsible for the ventricular patterns More central neurohumoral mechanisms probably play an important role here as well but are incompletely understood There is ample electrocardiographic documentation of these arrhythmias Rather striking RS T segment and T wave changes have also been shown to occur under similar stressful situations The latter have been of sufficient magnitude at times to suggest transient myocardial ischemia[11,13,14]

The arterial blood pressure closely reflects changes in feelings and attitudes Ballistocardiographic and cardiac catheterization studies on subjects deliberately exposed to emotional stimuli have disclosed major alterations in circulatory dynamics which disappeared when they were calm and relaxed[11,15,16] In some cases there was a distinct drop in arterial blood pressure often accompanied by a sinus bradycardia and occasionally by a sharp decrease in peripheral vascular resistance that culminated in full fledged vasovagal syncope More commonly however the blood pressure rose and either of two pressor patterns was seen One the so-called "cardiac output" pattern consists

mainly of a rise in systolic pressure that results from an increased heart rate and cardiac output and a decreased peripheral resistance. This closely resembles the hemodynamic changes produced by epinephrine. The other pressor response is characterized by an elevation of both systolic and diastolic pressure levels, relatively minor variations in cardiac output but impressive increases in peripheral vascular resistance. This "peripheral resistance" pattern parallels that induced by norepinephrine.

Feelings of anger and aggression are reported to be associated with the rise in blood pressure, whereas states of sadness and dejection are accompanied by the reverse.[11,13] The "peripheral resistance" response was observed to occur when aggressive feelings were inhibited, whereas the more common "cardiac output" pattern predominated when such feelings were overtly expressed. These interesting correlations demand further confirmation. Nevertheless, it is well established that the cardiac output can at least be doubled, the systolic and diastolic pressures increased to hypertensive levels, and the peripheral resistance raised by 50% or more during intense emotional reactions.[11,17] It is noteworthy that these circulatory responses are not necessarily abolished or significantly modified after thoracolumbar sympathectomy.[11]

Related renal blood flow studies, using the para-aminohippuric acid technic, have demonstrated a common reaction pattern to emotional stimuli. This consists of a fall in the effective plasma flow, a rise in the filtration fraction, and minor variations in the glomerular filtration rate.[11,18] These psychophysiological changes are in the order of 10 to 30% of the resting levels and have occurred in response to both spontaneous and deliberate emotional provocation. They have been shown to persist for considerable periods after the provoking stimuli have been removed, particularly in hypertensive subjects, and may long outlast the associated rise in blood pressure. Sympathectomy can abolish this renal reaction pattern, presumably by preventing efferent arteriolar constriction, yet the rises in blood pressure may still occur during stressful situations. Emotionally induced pressor responses thus do not appear dependent on either an intact sympathetic nervous system or on the kidney's vasoconstrictive ability.[11] There is need for further clarification of the pathogenetic potential of these cardiovascular-renal phenomena and their underlying mechanisms.

It has been reported that these pressor patterns are associated with an increase in blood viscosity and a decrease in the clotting time.[11] Epinephrine is known to accelerate the clotting time, but whether there are other mechanisms importantly involved here as well has yet to be determined. The theory has been advanced that these transient changes, if repeatedly produced, may come to persist for longer periods and predispose to intravascular thrombosis.[11,17] This hypothesis merits further investigation.

The apprehensive patient with cold, clammy hands and feet is familiar to all physicians. Marked peripheral vasoconstriction has been shown to occur with various changes in mood and mentation, often with concurrent vasodilatation about the head and neck.[2] These phenomena are minimized by centrally acting sedatives and disappear during sleep.[1] They appear to be initiated by central cortical processes and mediated by the sympathetic pathways.[2] It is common knowledge that emotional forces are among the important precipitants of such syndromes as Raynaud's disorder,[2] tension and periodic vascular headaches,[23] and certain types of generalized urticaria.[24] The underlying neurovascular and neurohumoral mechanisms, however, are far from clear.

PSYCHOPHYSIOLOGICAL MECHANISMS

For many years the sympathetic and parasympathetic pathways were held primarily responsible for these psychophysiological phenomena. Thus arose the concept of autonomic imbalance from which there developed terms such as "sympathicotonia" and "vagotonia." It gradually became evident that these two divisions of the autonomic nervous system did not function in simple opposition

to each other, and this concept finally fell into disrepute with the recognition of the regulatory role of the hypothalamus in peripheral autonomic functions. It has become evident, too, that the higher neural centers, and the hypothalamus in particular, have much to do with the regulation of endocrine activities, as is most clearly exemplified by the important hypothalamic pituitary interrelationships.[24-26]

The role of the endocrine system in the bodily responses to stressful stimuli is now common knowledge.[27,28] That the circulation can be profoundly influenced by hormonal factors is evidenced by the cardiovascular sequelae of epinephrine and norepinephrine, and hemodynamic effects of various thyroid extracts. Excess of corticotrophin and certain adrenocortical steroids, especially aldosterone, have been shown to produce impressive electrolyte and hypertensive changes.[28,29] Such neuro-endocrine mechanisms appear to be involved in the striking diuretic, metabolic, and electrolytic phenomena exhibited by some subjects during emotionally disturbing situations.[30] These may well be the mediating mechanisms whereby psychic forces can precipitate diabetics into acidosis and cardiacs into congestive failure.[30,31]

The hypothalamus is strategically located to discharge its responsibilities in the regulation of autonomic and endocrine functions. Evidence is accumulating, however, to suggest that the hypothalamus is in turn under the control of still higher autonomic centers in the cerebral cortex.[32-34] Importantly implicated here is a large cerebral convolution lying deep within the fronto temporal region. This is called the limbic lobe because it encircles the hilus of each cerebral hemisphere. The limbic lobe is a primitive cortical structure, common to all mammals, that contains a number of important centers, such as the cingulate and hippocampal gyri, the hippocampus, and the pyriform area. It shares many connecting pathways with the hypothalamus, amygdala, and other subcortical cell stations, and the entire complex is called the limbic system. Stimulation of the limbic cortex, by chemical and electrical technics, produces many of the visceral (and cardiovascular) phenomena that accompany emotional reactions. Ablation of this area results in a drastic reduction in emotional capacity and a disruption of many vital homeostatic mechanisms. This primitive lobe appears to function as the central psychophysiological authority, much as the surrounding neocortex presides over the higher intellectual activities. The delineation of this limbic system, and its distinction from the neocortical mechanisms, has provided us with a tangible anatomical and physiological basis for the circulatory and other visceral changes that accompany emotional responses.

THE SIGNIFICANCE OF PSYCHOPHYSIOLOGICAL PHENOMENA

Man's capacity to feel, as well as reason, contributes a unique and often intense quality to his otherwise colorless intellectual functions. Emotional responses bear importantly, too, on the nature and efficiency of man's defenses against noxious forces of all types, from the impact of a machine gun or the invasion by microbes to the intrusion of a mother-in-law.[27,17] For example, one's intellectual appraisal of a threatening situation is immediately colored by an intense emotional reaction (e.g., anger or fear). This emotional component of the reaction is essential to the physiological changes (e.g., the outpouring of epinephrine, the rapid conversion of liver glycogen to glucose, the tachycardia and increased cardiac output, the shunting of blood to skeletal muscles, etc.) that maximally mobilize the bodily forces for action. Such psychophysiological responses are clearly purposeful and have been called "protective reaction patterns."[35] There are believed to be many such patterns, featuring local or diffuse changes involving any or all organs and tissues.[17] Some facilitate offensive activity, whereas others serve defensive tactics. In some situations certain structures may respond excessively, whereas in others their functions may slow to a virtual standstill.

Many of these protective devices were undoubtedly vital to primitive man in his constant struggle with the many dangers of his

hostile environment. Modern man has less actual need of these mechanisms; nonetheless they appear to have persisted as part of his heredity. Wolff believes that they tend to become displaced in our present society and are more often induced by threats and symbols of danger than by true emergencies per se.[17] This, he indicates, is most likely to occur in situations perceived as threatening by virtue of their association, consciously or unconsciously, with earlier sensitizing experiences. For example, responses to various parental conflicts developed during an individual's formative years are likely to be evoked again during his subsequent encounters with authoritative figures, whether at school, at work, or in the military. As a simple illustration, consider the clinical patterns of vomiting and diarrhea that children commonly exhibit in response to illnesses of various types, infectious, emotional and otherwise. Given an individual who has been so sensitized as a child (e.g., by the insistence of an obsessive mother on a distasteful rigid dietary or a ritualistic bowel regimen) he is predisposed to utilize this "ejection riddance" reaction pattern again when he feels beset by threatening situations in adult life. Wolff and collaborators have delineated a variety of analogous reactions involving most of the body systems and functions.[17] In their experience these bodily responses are often inappropriate both in kind and magnitude to the current inciting stimulus. Nonetheless, so long as the disturbing forces continue, the emotional and bodily patterns tend to persist. It is in this way, Wolff states, that primitive protective patterns originally intended for actual emergencies are inappropriately evoked by experiences perceived as threatening and thereafter perpetuated into chronic states. The organs and tissues so involved initially exhibit disturbances of function only, but eventually, Wolff postulates, structural damage can result. These emergency mechanisms, though vital, have therefore been viewed as potentially pathogenetic. They function quite efficiently for short term needs. When, however, they are abused by excessive and prolonged demands, they may, like a two-edged sword, so strain the body economy as to derange and perhaps even destroy the very organism they were designed to protect. This is a plausible and provocative concept. The supportive data were derived from carefully constructed but, it should be emphasized, relatively short term experiments. Whether or not, therefore, these transient psychophysiological phenomena are truly the pathogenetic prodromata of serious structural disease will be for the future to determine.

PSYCHOPHYSIOLOGICAL SEQUELAE

There is no consistency in the way different individuals respond to the same stressful stimulus. The major factor determining our responses is the special emotional significance that a specific situation has for us. There is thus marked individual variation in the frequency and intensity with which psychophysiological mechanisms are called forth and, therefore, in their tendency to be perpetuated into chronic patterns. The relative importance of genetic and acquired factors in the production of these patterns is not clear, though it is probable that both are always involved to some degree.

Even though the full pathogenetic potential of these complex bodily reactions has still to be defined, they are clearly capable of causing considerable disability by virtue of the excessive concern and apprehension they usually produce. This is especially true for those phenomena that implicate the cardiovascular system. Medical errors of omission and commission may subsequently foster the patient's fears and prolong his ill health. Many subjects have become so health conscious in this way that seemingly trivial stresses have been capable of inducing major psychopathological sequelae.

For patients with pre-existing circulatory disease the potential consequences are much more serious. Individuals with coronary atherosclerosis may develop angina pectoris or an acute myocardial infarction when emotionally disturbed.[2] The impact of emotionally induced tachycardias and arrhythmias and abrupt alterations in stroke volume and peripheral vascular resistance appear quite

capable of disrupting an already impaired relationship between coronary supply and myocardial demand [1, 45] Concurrent changes in blood viscosity and clotting time may also contribute importantly here [1]

It has been reported that the additional burden of emotional stress was capable of precipitating frank congestive failure in the majority of a group of patients with the usual spectrum of chronic heart diseases [11] These clinical observations are supported by recent cardiac catheterization studies on similar subjects which revealed that anxiety could produce as potent hemodynamic changes as physical exertion and in a like fashion could alter the cardiac index in the direction of decompensation [16]

Patients with essential hypertension are often completely asymptomatic When symptoms do occur they commonly reflect the patient's level of emotional tension more than his vascular hypertension [11, 3] Relatively long term studies have revealed that the *blood pressure variations in hypertensives* correlate better with emotional factors than with any other single known influence [13] Short term experiments have documented the ability of emotional stimuli to induce the *hemodynamic changes of the hypertensive* state in normal subjects and to accentuate them in hypertensives [11, 3] There is considerable evidence that such reactions are mediated by the same neuro endocrine mechanisms *that according to* current concepts are fundamentally involved in the pathogenesis of essential hypertension [11, 1, 6] Less well documented are a number of case reports suggesting that these psychophysiological processes are often the critical determinants in the conversion of a benign hypertensive state into a malignant one Emotional factors may thus contribute *importantly to the development* and direction of hypertensive disease but their precise role remains to be fully clarified

Somatopsychic sequences as exemplified by the responses of patients to the diagnosis of cardiovascular disease are another important aspect of this general problem These are far more common more intense and longer lasting than is generally appreciated [30] The unexpected diagnosis of heart disease especially when the *symptoms are severe and of sudden* onset may provoke sufficient panic to induce an acute coronary occlusion or pulmonary edema Furthermore the patient's disturbed emotional state may limit his ability to cooperate and interfere *in general with the treatment* program Acute cardiovascular insults may also alter the cerebrovascular dynamics and lead to serious neurological and psychological sequelae

Many patients with *chronic heart disease* have considerable difficulty in accepting their disease and the limitations it imposes on them in a mature and realistic manner The physiological reflections of their sustained anxiety tension or depression may rapidly deplete an already reduced cardiovascular reserve Latent or mildly overt neurotic tendencies may be uncovered or exaggerated to the detriment of the patient in general and his heart disease in particular Of special interest is the so-called "denial of illness" pattern [30] Here the significance of the cardiovascular process *is so frightening to the patient that as a de*fensive psychological maneuver against his excessive anxiety he attempts to act out the pretense that he really has no heart disease He may go to the extremes of refusing or "forgetting" *to follow his therapeutic regimen*, and he may attempt strenuous physical activity in a vain effort to deny his cardiac diagnosis Such self destructive behavior poses a trying treatment problem indeed For patients with such tendencies it requires little iatrogenic impetus to convert a minor cardiac disorder into a major disability This applies *particularly to patients with coronary artery* disease who almost always become unduly apprehensive about their circulatory functions

FUNCTIONAL CIRCULATORY SYNDROMES

Through the years such diagnoses as *Irri*table Heart Disordered Action of the Heart Soldier's Heart Effort Syndrome Neurocirculatory Asthenia Cardiac Neurosis Autonomic Imbalance etc have been applied to those *cardiovascular syndromes* which developed on a so called functional basis However these

descriptive and supposedly etiological terms have tended to confuse rather than clarify the true nature of the problem

When examined closely the clinical features of these syndromes are found to be remarkably similar and there is now good reason to believe that their basic mechanisms are similar if not identical[6 34] Their characteristic manifestations of palpitations and precordial pain tachycardias and arrhythmias and variable degrees of peripheral vasomotor lability clearly implicate the cardiovascular system Their total clinical pictures however usually include other features of varying prominence such as dyspnea and tachypnea dizziness and syncope excessive weakness and fatigue gastrointestinal disturbances low grade fevers bizarre pains and paresthesias and various affective alterations It has thus become evident that these supposed cardiac states are actually multisystem disorders which suggests at once that the higher neuroendocrine controls of the visceral and emotional functions are involved in their genesis

Several years ago Friedman introduced the concept of cortico hypothalamic imbalance" to describe the central mechanism underlying these functional cardiovascular disorders[6] This state of imbalance develops he suggested when the special cortical areas controlling hypothalamic activity are either weakened or overwhelmed from within or without or when the hypothalamus per se is able to break away from its usual cortical restraints It is then possible he postulated for undisciplined hypothalamic discharges to induce these characteristic psychophysiological phenomena

Current neurophysiological concepts suggest that such a crucial central relationship would more likely involve the highest levels of the phylogenetically new and old brains that is the neocortex and the cortex of the limbic lobe[3 34] Thus one might envision a cortico cortical rather than a cortico hypothalamic linkage which when disrupted would then either provoke or permit hypothalamic dysfunction There is now increasing clinical and experimental evidence that such a key relationship does indeed exist and that dysharmony at this level is fundamental to most psychophysiological disorders[34] Much less clear however is our understanding of the noxious forces that are capable of disrupting this cortico cortical equilibrium and of the various factors that determine the special clinical features in individual patients

HYPERVENTILATION SYNDROMES

Hyperventilation is one mechanism responsible for many of these functional cardiovascular patterns that we have come to understand reasonably well[38 39 14] Acute hyperventilation syndromes are well known and are characterized by obvious overbreathing that classically culminates in frank tetany The chronic hyperventilation syndrome is far more common but until recently has not received just recognition[38 14] It tends to mimic closely serious organic disease and is particularly prone to masquerade as a cardiovascular process

Hyperventilation syndromes generally have a psychological basis Organic causes are uncommon but patients with cardiac disease frequently develop an emotionally induced hyperventilation pattern Such mixed" cases present complex diagnostic and therapeutic problems Chronic hyperventilation syndromes have the same clinical features as functional circulatory syndromes in general The cardiovascular manifestations are usually disproportionately prominent and tend to camouflage the multiple background symptoms referable to other body systems The clinical course tends to be punctuated by recurring acute hyperventilation attacks These patients tend to become acutely and apprehensively aware of their cardiac symptoms yet they may virtually ignore other concurrent phenomena For example and quite paradoxically they are often relatively unaware of their disordered breathing even though this is generally apparent to the observer Respiratory symptoms are thus not often emphasized by the patient despite their fundamental role in the genesis of the disorder

Regardless of the precipitating factors overbreathing is the initial link in the pathogenic chain of events These subjects are able to reduce their arterial carbon dioxide tension be

low a critical level very rapidly. They can usually lower their resting carbon dioxide tension by 50% or more within the first 30 to 60 seconds of hyperventilation.[39 14] This abruptly induces diffuse biochemical, neurovascular and neuromuscular changes which underlie the multiple clinical manifestations. The onset of these alarming phenomena, in turn, characteristically evokes excessive apprehension which tends to enhance and prolong the overbreathing. It is in this way that a cyclic, self-perpetuating process appears to become established.[14] This secondary fear response seems to be accompanied by an acute neuro endocrine discharge that complicates further the total clinical picture.

Recent studies have revealed that the rapid drop in arterial carbon dioxide tension substantially decreases the peripheral vascular resistance and lowers the arterial blood pressure by a direct effect on the vascular wall.[40] This abrupt pressure change, in conjunction with certain suspected electrolyte shifts (especially in the potassium and calcium concentrations) and the physiological sequelae of the patient's fear, are believed to cause the tachycardias and electrocardiographic changes that usually occur.[14] The sharp, stabbing type of precordial pain is common and has been correlated at various times with the onset of cardiac arrhythmias, diaphragmatic spasm, and gaseous gastric distention.[6 41] Often there is a dull and more enduring chest ache that appears related to relatively prolonged intercostal muscle spasm.[38]

The frequency of the brain waves decreases as the arterial carbon dioxide tension falls, and when this slows below five cycles per second there is some disturbance of conscious awareness.[39] This ranges from mild faintness and dizziness to complete loss of consciousness, although the latter occurs infrequently.

Peripheral and perioral paresthesias are a hallmark of the syndrome and, together with the muscular tremors and spasm, are linked with the abrupt neurovascular and electrolyte alterations.[42] Changes in the plasma potassium and ionized calcium concentrations are suspected of being importantly involved here.[42 14] Occasionally the myalgic and paresthetic patterns are asymmetrical and, rarely, may even be unilateral.[14 38] Such asymmetry is likely determined by hysterical mechanisms and, when the left upper extremity is so involved, the anginal syndrome may be very closely simulated.

Gastrointestinal complaints are common but seldom prominent. There is generally excessive oral dryness and frequently a pharyngeal tightness of the globus type. The triad of bloating, belching and flatulence is often present and results from the aerophagia that commonly accompanies the overbreathing. Occasionally these gastrointestinal symptoms are so prominent as to suggest cholecystic disease or an atypical anginal pattern.

Respiratory symptoms, when mentioned, may initially suggest a true dyspnea rather than a hyperpnea. Close questioning, however, will reveal this to be a subjective sensation of breathlessness and a difficulty in obtaining a full, satisfying breath. The patient will often indicate, by encircling his lower thorax with his hands, that his breath feels cut off at that level. Recent fluoroscopic studies suggest that diaphragmatic spasm may be the important underlying factor here.[41] These cardiorespiratory symptoms are not directly related to exertion. The patient will generally admit that they tend to occur *after* a strenuous, tension-filled day. This is significantly different from angina pectoris which characteristically begins *during* rather than after effort.

An acute exacerbation of the chronic hyperventilation syndrome usually develops in this sequence. The patient is preoccupied with some disturbing problem and begins to overbreathe without being particularly aware of so doing. When his arterial carbon dioxide tension drops sufficiently the resultant symptoms suddenly gain his attention and he becomes alarmed. He then begins to breathe even more vigorously and, generally for the first time, is conscious of some respiratory dysfunction. The breathlessness thus comes to be regarded as an unimportant sequel of the attack and the patient contends that it occurred *after* rather than before the onset of his alarming episode.

These patients usually manifest some degree of emotional distress. The anxiety and tension may be masked, in certain hysterical subjects,

by an inappropriate facade of pseudocalmness There are generally a number of nonspecific tension features in the background such as weakness and easy fatigability sleep disturbances increased irritability and impairment of concentration

Because the characteristics and course of this chronic hyperventilation mechanism have not been widely appreciated and because the patients do not often emphasize and properly relate their respiratory features, frequent diagnostic and therapeutic errors have resulted [14] Many patients have been needlessly disabled for many years by the erroneous impression that theirs was a cardiac affliction for which nothing could be done Recent experiences with a large group of such subjects have clearly demonstrated that even for those with many years of chronic hyperventilation it is generally possible to achieve dramatic and apparently sustained remissions with relatively simple and short term therapeutic methods [14]

Hyperventilators exhibit abnormal clinical and physiological responses to overbreathing [14] They possess a hair trigger mechanism for rapidly reducing their arterial carbon dioxide levels This may explain why as contrasted with normal subjects under identical circumstances their symptoms are so severe and develop so much earlier They also demonstrate more marked cardiorespiratory and acid base balance changes which they seem unable to regulate as efficiently as the normal individual They characteristically become very fearful with each exacerbation of hyperventilation and thus reinforces and perpetuates their undesirable psychophysiological cycle In a sense they have developed a more "efficient" respiratory mechanism but they lack unfortunately a parallel ability to compensate for the physiological sequelae of their ventilatory vacillations The conditioning effect of the repetitive overbreathing pattern appears to be a vital factor in the genesis of this syndrome [14] The therapeutic results suggest that this may be more important than any genetic or constitutional determinants

This conditioning mechanism has been used as a therapeutic tool both at the physiological and psychological levels After a thorough history physical examination and all necessary laboratory tests have been completed the subject's characteristic symptoms are dramatically reproduced by 1 to 2 minutes of voluntary overbreathing and are then quickly terminated by having him rebreathe from a paper sack. This initial therapeutic step is vital to an effective doctor patient relationship and appears to have a potent "deconditioning" effect It demonstrates impressively to the patient the reality of his symptoms yet simultaneously serves to convince him of their psychophysiological origin This is immediately reinforced by appropriate explanation of the benign nature of his illness and by reassuring instructions regarding the ease with which any future attacks can be controlled These therapeutic maneuvers may seem superficial to some but they have been shown to be crucial to the extinction of this unhealthy respiratory habit pattern The subjects subsequently have few hyperventilation attacks and can generally control them quite promptly if and when they do recur To the patient this is most reassuring His residual fears subside and his feelings of security and self confidence are proportionately strengthened

Approximately 75% of chronic hyperventilators can be expected to respond to such treatment with enduring remissions [14] Another 15% may require periodic reassurance to prevent any relapse during times of excessive emotional duress There are about 10% who derive little or no benefit from this approach These are usually individuals with marked hysterical or depressive mechanisms whose deep-seated difficulties demand formal psychiatric therapy

DISCUSSION

The bodily changes that accompany emotional reactions are many and varied Psychocirculatory syndromes are particularly common and have been clinically recognized as such for centuries The relatively recent elucidation of the neuro endocrine mediating mechanisms especially the limbic system has clarified considerably the anatomical and physiological basis of these phenomena

There still remains, however, much to be learned about these mechanisms and their pathogenetic capacity

We do know that the various changes in heart rate and rhythm, in blood pressure, and in peripheral vascular tone, etc, can be most disagreeable and alarming Considerable disability may thus result in otherwise normal individuals especially if there has been an erroneous diagnosis of organic disease For many subjects the impact of such iatrogenic trauma may have major physical, psychological, and socio-economic repercussions

Patients with cardiac abnormalities of minor functional significance are particularly susceptible to this undesirable sequence of events The writer clearly recalls a woman of 31 who had been kept bedfast since the age of 16 when a loud murmur, stemming from a small septal defect, was accidentally discovered It required Herculean efforts to rehabilitate this patient which, fortunately, was finally achieved Although now happily married, and the mother of two healthy young children, she can never be recompensed for her 15 lost years Such tragedies are far better prevented than belatedly treated

These psychocirculatory phenomena are potentially more threatening for subjects with serious cardiovascular disease Under the impact of emotional stimuli they may be precipitated into acute congestive failure or be stricken with an anginal attack, myocardial infarction and, not uncommonly, sudden death There is now virtually general agreement as well that psychic *forces bear im*portantly on the clinical characteristics and course of the hypertensive state Some believe that psychological mechanisms may be crucial to many of the serious sequelae of this syndrome

So called somatopsychic sequences are another variation on this general theme It is a common clinical observation that many patients, when abruptly confronted with a cardiovascular diagnosis, may react with marked physiological, psychological and behavioral changes Not only can such intense reactions adversely affect the primary circulatory process but, and this is not well enough appreciated, the traumatic impact on the patient as a whole may seriously disrupt the total treatment program

It is now quite clear that the various functional circulatory syndromes, irrespective of their diagnostic labels, are actually multi system processes whose cardiac features merely occupy the clinical foreground We have, in consequence, become much more interested in the fundamental neuro endocrine mechanisms involved here than we are in the visceral end organs, despite the apparent clinical prominence of the latter Indicative of these changing views are the recent concepts of cortico-cortical and cortico hypothalamic imbalance which emphasize the psychopathological sequences that seem to underlie these disorders

There is a common tendency to confuse the terms "psychogenic" and "psychosomatic," and to use them interchangeably In actual fact, however, they are not synonymous The latter signifies only a correlation in time between emotional and bodily changes without necessarily implying a causal connotation Conversely, the term "psychogenic" conveys the idea that bodily changes have been caused by emotional forces Such an etiological concept has still to be confirmed At the moment we can say only that alterations in feelings and in bodily functions tend to occur together as related facets of a total response pattern In other words, it is the writer's contention that "psychosomatic," properly used, should refer only to changes in psychological and visceral functions that occur more or less *concurrently in response to some stimulus*, whereas "psychogenic" suggests a causal sequence, e g, stimulus→psychic change→visceral change, that has yet to be proven The comments to follow on the relevance of conditioned reflex mechanisms to psychophysiological processes cast additional light on this concept The ultimate capacity of these mechanisms has yet to be fully defined

Past medical generations tended to think in terms of a single cause for a specific illness The concept of multicausality, now generally accepted has rendered this viewpoint obsolete We know, for example, that poliomyelitis or rheumatic fever do not develop as the result of a particular virus or special

streptococcus alone Other pathogenic factors must pave the way for a successful invasion by these organisms There is little doubt that all are exposed to and probably invaded by them, yet few exhibit the clinical syndromes Moreover, of those who do fall ill it is only the occasional individual who develops any of the serious sequelae And finally only a fraction of the latter succumb to their illness We realize now that states of health and disease depend upon the complex interplay between multiple forces e g (1) the precipitating factor or factors together with a number of contributory or modifying influences (2) the biological make up of the individual including the various determinants of his relative resistance or susceptibility and (3) the pathophysiological mechanisms initiated by the interaction between the individual and the forces with which he is beset

The very nature of man's intellectual and emotional endowment introduces of necessity a psychophysiological component either primary or secondary in nature among those factors and mechanisms bearing on his illnesses Thus there are no pure organic or psychological processes per se Rather in any given illness there are always a variety of forces psychological and otherwise that determine its development and the course it will follow

When contemplating this matter of mind body relationships the layman and unfortunately many physicians as well commonly consider physical and psychological mechanisms as fundamentally different phenomena The fallacy of this prevalent misconception was recently emphasized by Stanley Cobb who said "*Mind* is an abstraction denoting the active integration of the billions of nerve cells and hundreds of nuclei of the living brain It depends for its normal function upon the homeostatic mechanisms of the whole body The brain is continually passing nerve impulses from one group of nerve cells to another These are messages At lower levels they have to do with more simple functions like breathing digesting and locomotion At higher levels they reach an incomprehensible complexity and deal with symbols concepts and memories But the principle is the same as at the lower more reflex level sensory stimuli arouse stored conditioned responses memories are brought in symbols are constructed and the whole communication mechanism is channeled to a motor outlet to cause behavior It is the integration in action the relationship of one part of the brain to another that is mind Mind is as much a function of the brain as contraction is a function of muscle It is merely so complex that it is difficult to comprehend "[4]

These functional phenomena ascribed to alterations in mood and mentation are thus seen to have as respectable" an organic basis as the varied manifestations of all other disease states Man is an indivisible albeit complex unit and as he must reacts to forces of whatever nature as a psychosomatic entity His feelings and his bodily functions are inseparable they merely represent individual though interrelated facets of the same basic phenomenon The perceptive medical approach therefore is that which encompasses all the relevant factors and is not impaled on the horns of a man made "either organic or psychogenic dilemma

There remains however much to be learned about the nature of the emotions and their associated bodily changes We have yet to fully fathom the factors that determine which particular structures will be involved and what symptoms will be prominent in various emotional responses There is need for further clarification of the relationships between different feeling states and the bodily phenomena that accompany them Wolff and his colleagues have made some interesting observations in this regard although their correlations have been criticized on the basis that they considered mainly their subjects conscious feelings with insufficient attention to their repressed emotions The validity of their formulations therefore must await future confirmation We know little too of the mechanisms whereby specific symptom patterns are as it were chosen by different individuals from among the diffuse physiological changes that they experience Just why the tensions of one person are reflected mainly by his cardiovascular system whereas the gastro

intestinal tract is prominently involved in another is poorly understood

The role of genetic and constitutional factors remains quite obscure To the writer, however, it seems both sterile and stifling to consider these the crucial determinants of man's psychophysiological behavior Environmental forces also exert an important influence on the development of our characteristic behavior patterns, at times uncovering or augmenting certain inherited tendencies, and on other occasions minimizing or thwarting their overt expression Various inborn tendencies may thus be cultivated or curbed by the modifying effects of meaningful environmental experiences

There is now increasing evidence that conditioned reflex mechanisms are prominent among the environmental processes concerned with the formation of our behavior patterns Liddell's ingenious studies on the sheep and goat have clearly demonstrated the pathogenetic potential of these conditioning procedures, particularly during the early period of the organism's development[44] He has clearly illustrated as well that influences as diverse as hormonal changes or the location of the mother animal during the experimental procedure may markedly modify the expected results Gantt has successfully used similar conditioned reflex technics to induce specific visceral responses in the dog, such as impressive tachycardias and arterial hypertension[45] He has observed that a conditioned cardiac reflex may persist long after a somatic reflex, conditioned by the same stimulus, has become extinguished In other words, it appears that conditioned visceral responses may be "learned" better and persist longer than those related to the voluntary neuromuscular apparatus MacLean has pursued the problem further and has shown that these visceral responses rely importantly on limbic system mechanisms[44] Moreover, he has found that Rauwolfia preparations can selectively depress limbic functions and are thus capable of abolishing such conditioned cardiac reflexes In an unrelated clinical study on subjects with coronary artery disease, the majority were noted to experience a marked decrease in the frequency and severity of their anginal attacks after the administration of Rauwolfia[46] In some subjects this improvement persisted for prolonged periods (weeks to months) beyond the known pharmacological activity of the drug The obvious implication here is that a conditioned reflex mechanism may be operative in the genesis of the anginal syndrome and that this, at least for a time, may be dampened by the depressant effect of Rauwolfia

These observations quite naturally have raised the question as to whether the repetitive impact of stressful environmental stimuli might bear importantly on the genesis of various cardiovascular syndromes It certainly seems both possible and plausible that brief, discrete vascular responses, if evoked often enough during an appropriate developmental period might develop in time into a persistent pathophysiological pattern requiring progressively less reinforcement to be maintained This is somewhat analogous to Wolff's concept of the conversion of our primitive protective reaction patterns, originally intended for short term emergency needs, into unhealthy "ways of life"[25,17]

The future promises to disclose exciting discoveries in this area of psychophysiology At the moment we can see only the general shape of things to come, but the complex details are certain to be slowly and steadily revealed as man's inherent curiosity and quest for knowledge continues

THERAPY

It is not within the scope of this chapter to delve deeply into therapeutic methods Brief mention is warranted, however, of some general principles and concepts that have practical value for the nonpsychiatrist

At the outset it should be clear that the appraisal and management of emotional factors are important adjuncts to, rather than substitutes for, traditional medical measures The role of such factors varies considerably from case to case, and treatment must be tailored, as always, to the individual patient's needs

The keystone of all therapy is the quality of the patient physician relationship It is to

be emphasized that this type of treatment is not an intellectual exercise wherein the physician imposes his wisdom and wishes on the patient. It must be viewed rather as a psychological experience during which the patient is helped to achieve some measure of emotional readjustment and reeducation. Man has an amazing ability to alter his attitudes and beliefs and thus his ways of contending with the problems and pressures of his daily life. The physician's presence and personality are the vital catalysts in the mobilization of the patient's resources and his basic drive to help himself. Sensitive clinicians may thus achieve impressive therapeutic results without a profound knowledge of psychopathology. As tangible evidence of this are the gratifying responses of the subjects with hyperventilation mechanisms and on a broader scale those reported by Wolff and his group from their special experimental clinic at the New York Hospital.[14-17]

Theoretically there are two broad forms of psychotherapy: (a) expressive or uncovering and (b) suppressive or covering. In actual practice there is usually involved an admixture of both. Expressive therapy requires skilled personnel and utilizes specialized methods that are beyond the scope of the average physician. Suppressive therapy, on the other hand, is usually well within the therapeutic domain of the nonpsychiatrist. Although supposedly more superficial, it can be very effective. It functions within two main areas: (a) the manipulation of the patient and (b) the manipulation of the environment. As therapy potentially begins with the initial visit, the physician's warm and interested attitude is the primary important therapeutic step. This will encourage the patient to air his conscious problems and, if received properly, this will afford him significant relief. Reassurance and encouragement from the understanding physician will provide further support and help allay the patient's anxiety. Superficial insight into the relationship between his emotional problems and physical symptoms and appropriate simplified explanations of the underlying mechanisms will give the patient additional understanding and frequently dissolve many of his fears. When he appreciates that these disorders are extremely common, that everyone has a tolerance level beyond which he will break, the patient will no longer regard himself as a defective specimen and will begin to regain his self-esteem. In conjunction with these direct efforts it is often necessary to effect certain environmental changes so as to minimize the stressful factors impinging on the patient. For this purpose the relatives and other key persons in the patient's environment at home and at work may have to be consulted and their cooperation secured. Similarly, the services of various social agencies can and should be utilized. Many of these are able to render invaluable aid.

To some physicians these therapeutic maneuvers may seem too superficial to be effective. In actual practice the patient's responses testify that deep seated drives and feelings are being mobilized. These dynamic forces are catalyzed for good or for ill by the quality of the patient-physician relationship. Even though the physician may lack full understanding of all that is going on, these therapeutic technics can achieve satisfying and often dramatic results if suitable rapport has been developed.

Certain practical working principles should be observed by the nonpsychiatric physician. He should restrict himself to the discussion of material that is within the patient's conscious awareness. Though he may gain insight into more basic problems, the physician should avoid uncovering forces he cannot control. These may seriously disturb the patient. He should permit the subject to air his fears and feelings rather than "hold the floor" himself. He should avoid premature evaluations and advice lest he destroy the patient's confidence and, for the same reason, he should not render moral judgments and pointlessly criticize. He should not make decisions for the patient; this fosters only further dependency. Admittedly, patients cannot be "given" a mature and realistic perspective, but they most certainly can be "helped" to achieve it.

In closing, it should be noted that the physician in actual fact has little choice as to whether or not he will deal with these psychophysiological problems—his only choice

lies in whether he will handle them well or badly.[47] On this same theme it was Paul White who said: "Neither the psyche nor the soma should hold the limelight. They comprise but halves of the same circle, without beginning or end but with varying, alternating or even coincidental lengths of arc. We cannot well consider them separately. We must put the body together again."[48]

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CHAPTER 34

Rheumatic Fever: Its Nature, Diagnosis and Treatment

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THE VARIOUS *manifestations* of rheumatic fever have been recognized for centuries The integration of these findings to form the picture of the disease as it is recognized today has occupied whole lifetimes of many physicians over these same years Though we have today a fairly clear picture of rheumatic fever for descriptive purposes the detailed nature of the rheumatic state remains a loose network of poorly understood material

PATHOGENESIS

For many years it has been apparent that respiratory infections commonly precede the onset of rheumatic fever So consistent was this association with what was generally a severe pharyngitis that it was not until the Nineteenth Century that Cheadle made evident the distinction between diphtheria and rheumatic fever Andrews Derick and Swift suggested that the then quite prevalent streptococcal sore throats were those that were followed by rheumatic fever This remained in the realm of probabilities until 1931 when Coburn published the data included in his rather extensive monograph on rheumatic fever The variety of observations recorded in this volume have since been amply confirmed From Mackenzie's material Coburn notes that Beta streptococci may be recovered from the tonsillar tissue of 90% of children with rheumatic fever He showed further that in his own clinical material rheumatic fever followed documented Beta streptococcal infection By following with serial throat cultures patients with inactive rheumatic fever he first observed the striking recurrence rate that followed the acquisition of Beta streptococci in these patients He also correlated the low incidence of streptococcal infection in San Juan with the low incidence of rheumatic fever and showed that the incidence of rheumatic fever in New York followed closely the seasonal variation in streptococcal infections Similar observations were made simultaneously and independently in England by Schlesinger and others

Following these observations that group A streptococcal infections are intimately associated with the occurrence of acute rheumatic fever a mass of clinical epidemiological and immunological data supporting this concept were accumulated In addition as will be seen in the discussion to follow appropriate therapy and prophylaxis of streptococcal infection promise to reduce the incidence of initial attacks of rheumatic fever and have already reduced the rate of recurrences of this crippling heart disease Thus the translation of the theory of streptococcal etiology into an effective preventative measure serves to strengthen the concept that the two diseases are intimately related

In addition to the rather clear relationship between infection by group A streptococci and rheumatic fever there remain a number of other correlations the significance of which remains to be clarified

AGE

The great majority of cases of rheumatic fever occur between the ages of 5 and 15 years (Table I) with a mean age that has varied from 7 to 10 years in various studies. Rheumatic fever, however, is by no means restricted to children as has been shown by the extensive experience in the armed forces during World War II. The ages of greatest prevalence have long been known for their high incidence of respiratory disease and though age specific attack rates following streptococcal infections are somewhat meager, it appears that in children, as in adults, approximately 3% will develop rheumatic fever following untreated group A streptococcal infection (Table II). It may very well be, in spite of the long accepted view that rheumatic fever is a disease linked clearly to age, that the only significance of the high incidence of rheumatic fever among school age children is that this is also the age of highest incidence of group A streptococcal infection. Age, then, may be without real significance in the pathogenesis of rheumatic fever. Further studies on this important point are needed.

TABLE I
AGE DISTRIBUTION IN RHEUMATIC FEVER

	Age at Onset in Years 0–4	5–9	10–14	15 over	Onset All Ages
Acute rheumatic fever	9	154	182	15	360
With active heart disease	2	87	94	8	191

(Data of Conybeare, J Roy San Inst 71 301 1951.)

TABLE II
RHEUMATIC FEVER ATTACK RATES

Location	Streptococcal Illness	Number Cases	Percent of Cases Developing Rheumatic Fever
Denmark [8]	Tonsillitis	840	3.6 (mainly adults)
North Carolina [10]	Tonsillitis	100	3.0 (adult)
Boston [11]	Scarlet fever	102	3.8 (average 11.1 yr)
Wyoming [9]	Tonsillitis	1062	2.7 (adult)

SEX AND RACE DISTRIBUTION

No real differences have been demonstrated that cannot easily be attributed to some other factor. This equal distribution between the sexes is not as clear in those children with isolated chorea. In the latter disease it would appear that girls have a somewhat higher rate of occurrence. This may, however, reflect the nature of chorea. It seems quite logical to presume that, while some of the behavioral characteristics of chorea which might be tolerated in boys and not called to the attention of a physician, would represent distressing signs in girls and serve to bring them to the attention of a physician and permit establishment of the diagnosis. In our own clinical material the predominance of girls over boys in this respect is not striking. Interestingly enough, in light of the conflicting opinions concerning hereditary predisposition, there are no differences in the incidence of rheumatic fever attributable to racial characteristics.

SOCIO ECONOMIC FACTORS

Rheumatic fever has long been considered as a disease of the poorer classes and is closely associated with crowded and inadequate housing that is characteristic to various degrees of those receiving lower incomes (Table III).

TABLE III
THE SOCIAL INCIDENCE OF RHEUMATIC FEVER AND GROUP A STREPTOCOCCAL CARRIER RATES IN CHILDREN

Rental Area	Number of Cases 1938–1948	Cases per Year per 10,000 Children (5–14 yr)	Percentage Strep Carriers
High	202	4.7	12.5%
Medium	325	7.5	18.0%
Low	942	15.0	25.0%
Total	1469	10.1	

(Data of Holmes, J Hyg 51 450 1953.)

By contrast, the occasional occurrence of rheumatic fever in members of the population with a much better standard of living has been repeatedly documented. Factors of diet and sanitation appear to play no part in their own right. However, those epidemics of strepto-

coccal infection that have been milk or food borne provide the first part of the answer to the correlation between socio-economic status and rheumatic fever. Here it can be shown that the attack rate of rheumatic fever that follows such strikingly acute epidemics is not directly related to such factors as may be considered in socio-economic terms.

The incidence of streptococcal infection that may be attained in any population group is related primarily to crowding. This has been shown in various population groups and in the armed forces. The rather glaring exceptions to the correlation between crowding, substandard living conditions and rheumatic fever become meaningful in light of the virtual absence of streptococcal infections in some areas of the world. It may, however, be that in these areas rheumatic fever occurs in a form not recognized by our present clinical criteria, and further studies of incidence of streptococcal disease, overt rheumatic fever and occurrence of rheumatic heart disease need to be carried out.

GEOGRAPHICAL AND SEASONAL VARIATIONS

The geographical differences in the incidence of rheumatic fever again appear to be primarily a function of the incidence of streptococcal infection and though few studies are available of attack rates documenting association with streptococcal infection in these areas of low incidence, there is nothing to suggest that any evident differences exist. A great variety of seasonal differences have been reported. In some areas of the world streptococcal infection and rheumatic fever occur evenly distributed throughout the year. In Great Britain the period of greatest incidence of rheumatic fever occurs during the late fall and early winter months while in most areas of the United States the peak months are found in the late winter and early spring.

HEREDITY

This aspect of pathogenesis remains the most controversial of those factors that bear a close correlation with the incidence of rheumatic fever. It has been shown, however, that the attack rate following streptococcal infection is the same regardless of the presence or absence of a positive family history for rheumatic fever. It would appear that in those families where there is an inordinately high incidence of rheumatic fever, there is also a parallel incidence of streptococcal infections. The apparent familial incidence, then, as with those other factors previously discussed, may well be a function of the number of streptococcal infections that occur in these families. The same factors that influence the incidence of streptococcal infection then apply to the apparent hereditary predilection. Thus from the epidemiological studies that have been made there is no clear evidence for a hereditary susceptibility. The interest in this aspect of rheumatic fever has stimulated the search for a biochemical anomaly that could be demonstrated in the families of rheumatic individuals. It has been shown that in rheumatic families there is, in the siblings and parents of these children, both a low level of the non-specific hyaluronidase inhibitor and certain abnormalities in steroid levels. These abnormalities have been used as evidence of a hereditary defect that predisposes these individuals to rheumatic fever. It is equally possible that these biochemical abnormalities are a function of repeated streptococcal infections. It is evident that further investigation will be required before any clear understanding is achieved.

THE ROLE OF STREPTOCOCCUS IN RHEUMATIC FEVER

Though the intimate relationship between infections with group A streptococci and rheumatic fever has been well documented, the role played by the streptococcus in the production of rheumatic fever remains obscure. The various investigations attempting to establish the nature of the streptococcal effect may be grouped into four categories. There are, however, many observations which cannot be fitted into any category and these remain as isolated observations which only future investigation can link together.

There is reason to think that one of the

many cellular components or extracellular products of the group A streptococcus are directly toxic producing injury to tissues resulting in the manifestations of rheumatic fever Various components of the bacterial cell have been shown to be toxic for a variety of experimental animals but in none of the investigations have pathological lesions of rheumatic fever been reproduced In addition the various components of the streptococcus that have demonstrable toxicity vary widely in concentration in cultures of the various types of streptococci It must follow from the epidemiological evidence already presented that should some toxin be concerned in pathogenesis of rheumatic fever this substance would have to be produced in approximately the same amounts by all types of group A streptococci since the attack rate of rheumatic fever appears not to differ following infections with the different types of streptococci It has also been shown that in some fatal streptococcal infections the distribution of inflammatory lesions is similar to the distribution of the lesions in rheumatic fever Though the evidence to date is rather me... [illegible]

t [illegible] ...s of rheumatic fever remains an attractive and worthwhile line of investigation

It has long been felt by many that rheumatic fever has an allergic basis The superficial resemblance of exudative rheumatic fever to serum sickness strengthens this concept Both the distribution and the nature of the pathologic lesions lends support to this concept It is obvious however that the clinical manifestations of rheumatic fever and serum sickness as they occur in man are relatively easy to distinguish in most instances Indeed the differences between serum sickness and rheumatic fever are every bit as striking as the similarities Again the pathological lesions of rheumatic fever resemble other disease states i e periarteritis nodosa that are also considered perhaps on more substantial grounds to have an allergic basis The evidence for an allergic nature of any of these states is however far from substantial

The latent period between the streptococcal insult and the development of manifestations of rheumatic fever parallels the well known latent period between antigenic stimulation and the appearance of circulating antibody A very similar latent period however occurs prior to the appearance of diphtheritic myocarditis and the exotoxin concerned here is thought to be directly responsible for the lesions observed

Though the possible damage from the interaction of antigen and antibody within the tissues has become less attractive in recent years it has served to focus attention on such portions of the immune response as tuberculin or delayed type hypersensitivity Various experimental diseases would appear to hinge upon this facet of the immune response but none bear more than a very superficial resemblance to rheumatic fever There is however some evidence suggesting that rheumatic fever follows only after repeated streptococcal infections Only 8 of first attacks of rheumatic fever occur in children under 5 years of age and these are not years that are free from streptococcal infection The nature of streptococcal infection in this age group as Powers et al have shown differs from the typical stormy acute follicular tonsilitis which is produced by streptococcal infection in adults The rather insidious poorly differentiated illness that is characteristic of streptococcal infections in young children does not appear to be followed by rheumatic fever in its usual form It has been postulated that repeated infections are required before streptococcal disease takes on its characteristic adult pattern and before infections with this organism are followed by an appreciable incidence of nonsuppurative sequellae Though the evidence is not as clear as it might be various studies indicate that as a group those individuals developing rheumatic fever following a streptococcal infection produce more antibodies to streptococcal products than do patients having streptococcal infection This again suggests the possibility that repeated streptococcal infections are required for the development of rheumatic fever There is however overlap in each series of observations and certainly other possible hypotheses to account for the enhanced production of antistrepto-

coccal antibodies are equally cogent Murphy and Swift have presented experimental evidence for the role of repeated streptococcal infections in the development of a process in rabbits which they believed to be similar to rheumatic disease in man They were able to produce by repeated streptococcal infections lesions in the myocardium of the rabbit resembling those found in acute rheumatic fever in man These observations suggest that the immune response of the host must play some part both in the expression of streptococcal infection and in the development of rheumatic fever Such lesions as follow streptococcal infections might also be the result of the persistence of the streptococcus in these areas In the past however except for the reports of Green and Collis attempts to recover streptococci from these areas has yielded either equivocal or negative results In recent years though the description of the virus like L forms assumed by the streptococcus under certain cultural conditions has provided a new area for investigation It could well be that these forms are responsible for the lesion found in acute rheumatic fever Though these approaches to the pathogenesis of rheumatic fever remain attractive they too suffer from a lack of direct evidence

Over the years it has been attractive to many to consider rheumatic fever and related diseases to be the work of a virus infection Although no convincing evidence of this relationship has been presented the concept that a virus or bacteriophage accompanying certain strains of group A streptococci as they invade the tissues remains attractive and is the subject of continuing investigation The final category of investigation that attempts to define the nature of the rheumatic state is that initiated by Selye and in recent years extended by Kelley *et al* To Selye and his co workers rheumatic fever represents one of the diseases of adaptation featured by aberrant function of the pituitary adrenal axis Kelley and his associates have presented evidence suggesting that the rheumatic state may be defined physiologically as one of relative or as they term it segmental adrenal insufficiency They have demonstrated that patients with well established rheumatic fever have increased amounts of circulating ACTH and at the same time possess a low plasma concentration of 17 hydroxycorticoids This adrenal disturbance differs from Addisons disease and certain other anomalies of adrenal function since it is a quantitative defect as shown by the fact that these patients respond to stimulation by large amounts of exogeneous ACTH Here then if these observations be confirmed is evidence of a biochemical anomaly in patients with rheumatic fever The relationship of these observations to the role played by the group A streptococci in the pathogenesis of rheumatic fever remains obscure It is attractive to think of these changes as physiological alterations occurring as the result of repeated streptococcal infections Such changes however might also reflect either a direct toxic injury or an allergic state and much study needs be done to establish their physiological basis

PATHOLOGY

As is evident from the clinical manifestation a number of organs and tissues may be involved in the rheumatic process These are primarily the heart the periarticular connective tissue the brain the skin subcutaneous tissue and the membranes of the serous cavities The variability with which these areas are involved and the different combinations possible are as complex as is the disease itself Many consider the basic lesion to consist of fibrinoid degeneration of the collagenous ground substance At first a generalized swelling of the collagen fibers is said to occur which is closely followed by a loss of fibrillar structure and the ultimate formation of a homogenous eosinophilic material Superimposed on this basic injury there is generally a proliferative response which results in the formation of minute granulomata With this there is a mononuclear inflammatory exudate Histiocytes and occasional eosinophils are at times present and the characteristic "owl

eyed" mononuclear cells described by Anitschkoff are often prominent

The Aschoff body is the pathognomonic form that these lesions take when they appear in the *myocardium* They *may be found in the adventitia of the smaller arteries and* veins supplying the myocardium or they may be completely surrounded by myocardial fibers Similar lesions may be found in the loose connective tissue associated with the larger arteries The individual lesions are globular or elliptical and present as a central *area of fibrinoid degeneration with a surrounding collar of mononuclear cells* In what are believed to represent older lesions may be found large cells with abundant basophilic cytoplasm and nuclei containing a large prominent nucleolus These cells are often multinucleated The genesis of these lesions and the role played in their formation by de*generating myofibers is still not clear*

Subcutaneous nodules present another characteristic form of the granulomatous response observed in this disease These lesions have a central core of fibrinoid necrosis surrounded by an area of inflammation composed of large mononuclear cells in radial and palisade arrangement Multinucleated giant cells with prominent nucleoli are often observed *No distinct capsule is present and the periphery of the lesion is somewhat indistinct*

Rheumatic pneumonia constitutes another pathological process which is occasionally present in acute rheumatic fever This consists primarily of interstitial edema with capillary hemorrhages and the formation of hyaline (fibrinoid) membranes in the alveolar ducts There is an abundant cellular exudate composed primarily of mononuclear cells *Scattered areas of fibrinoid degeneration at times may be found in the connective tissue and arterial lesions are often present* Histochemical and immunochemical studies indicate that the fibrinoid material found at the site of collagen degeneration or in the granulomata mentioned above is fibrin or material closely related to fibrin but the process resulting in its deposition has not yet been defined

MANIFESTATIONS

The protean manifestations of rheumatic fever have been repeatedly emphasized since the early papers were presented describing the multiplicity of clinical phenomena that may occur in this disease The florid examples *of rheumatic fever that present no great diagnostic problem are not those that* at this time result in confusion The availability of a means of preventing recurrent attacks of rheumatic fever with their attendant high incidence of crippling cardiac damage de*mands* the accurate diagnosis of rheumatic *fever and the definition of borderline states*

This is not an easy distinction to make in many cases Following a streptococcal infection in addition to the small number of patients who develop frank rheumatic fever there occur another 5 to 10% who manifest *a great variety of minor findings during con*valescence that by most physicians would not be considered diagnostic of rheumatic fever However these changes seem to imply that an altered state of reactivity to streptococci or their products exists Because of the lack of specificity of these changes a danger exists that unrelated illnesses may erroneously be considered to be rheumatic fever *Obscure bacterial infections and certain viral diseases* at times *present* clinical and laboratory findings superficially resembling rheumatic fever It is for this reason that in the absence of the availability of a specific diagnostic laboratory test or pathognomonic clinical sign a *reasonably foolproof* scheme to aid diagnosis though it draws arbitrary lines can provide a most worthwhile service to the clinician For this reason the diagnosis of rheumatic fever today rests on constellations of clinical and laboratory criteria The accompanying tables *outline* the major and minor manifestations which have evolved *from the* original criteria for diagnosis of rheumatic fever presented by Jones In this scheme the presence of at least two major manifestations or [illegible]

TABLE IV

MAJOR MANIFESTATIONS USED IN THE DIAGNOSIS OF RHEUMATIC FEVER

Manifestations	*Remarks*
1 *Carditis*	
a) definite cardiomegaly	Demonstration of increasing heart size
b) significant murmur	Blowing apical systolic murmur localized or transmitted to axilla; Mitral or aortic diastolic murmur
c) pericardial friction rub	
d) cardiac failure	In a young child or adult (under 25) in the absence of other causes
2 Migratory polyarthritis	Objective findings of swelling, tenderness, erythema or heat
3 Subcutaneous nodules	
4 Chorea	
5 Erythema marginatum	

and two minor manifestations constitute minimum grounds for the diagnosis of rheumatic fever. It can be readily seen from studying these criteria that some illnesses unrelated to rheumatic fever will at times fulfill these criteria, and it is not always easy to distinguish from rheumatic fever such diseases as rheumatoid arthritis, anaphylactoid purpura or other "collagen" diseases. Sickle cell anemia and leukemia often present symptoms and signs consistent with the clinical diagnosis of rheumatic fever. However, if these criteria are considered to be exclusive as well as inclusive, relatively few mistakes in diagnosis will be made. For example, auxiliary findings are often seen in the other diseases mentioned and the course of the disease itself will generally serve to establish the correct diagnosis. At best, however, the accuracy of the clinical diagnosis of rheumatic fever is mediocre. Many cases of rheumatic fever must be excluded by insistence on the classical clinical and laboratory features and many cases representing processes based on other etiologic and pathogenic mechanisms are too frequently labeled rheumatic fever. However, in the absence of a specific diagnostic laboratory test or absolutely pathognomonic clinical sign, the criteria originally formulated by Jones and modified by the Rheumatic Fever Committee of the American Heart Association provide the best basis for avoiding errors of both omission and commission in the diagnosis of rheumatic fever.

The patient who presents to a physician a combination of minor manifestations occurring in the absence of major criteria following recovery from a streptococcal infection provides a challenge for which there is no satisfactory answer at the present time. These patients do not have what is commonly considered rheumatic fever but their illness obviously reflects an altered host response to streptococcal infection possessing similarities to rheumatic fever. With our present knowledge, in our clinic we have quite arbitrarily

TABLE V

MINOR MANIFESTATIONS USED IN THE DIAGNOSIS OF RHEUMATIC FEVER

Manifestations	*Remarks*
1 Fever	Rectal temp. over 100°F
2 Polyarthralgia	No objective findings present (includes history of arthritis). Must not be used as a minor manifestation when arthritis also considered as a major finding
3 Abnormal EKG	1st degree heart block or greater, abnormal P waves; QRS slurring, notching, widening, low voltage; *ST segment or T wave* alteration; Increased QTc
4 Abnormal acute phase reactants and anemia and leukocytosis	>20 mm/hr ESR by Westergren method; Positive C protein, elevated mucoprotein; WBC count >12,000
5 Evidence of preceding streptococcal infection	By history or serological means, bacteriological isolation
6 Past history of rheumatic fever or presence of inactive rheumatic heart disease	
7 Other manifestations as severe epistaxis, abdominal pain, pulmonary changes, weight loss	These manifestations provide additional evidence of the presence of rheumatic fever but are not to be included as diagnostic criteria

chosen to call this state a post streptococcal syndrome. We feel that it may be justifiable when such findings are present following a proved streptococcal infection to place these children on penicillin prophylaxis for 1 or 2 years. It is possible though by no means established that this syndrome represents a pre rheumatic state which if followed at some short interval by another streptococcal infection might result in full blown rheumatic fever.

CARDITIS

Of the several manifestations of rheumatic fever carditis is the most important both for diagnosis and prognosis. It may occur in such a mild form that it does not permit a clinical diagnosis during the acute phase of the disease and only makes its presence known during later life with the appearance of valvular rheumatic heart disease. For example approximately half of the patients with acute rheumatic fever will have carditis during the first attack of the disease. The diagnosis in the majority of these cases rests on a variety of heart murmurs that may be detected during this period. Many murmurs that occur during the acute phase of rheumatic fever are secondary to such factors as fever tachycardia anemia or cardiac dilatation and their intensity and quality is extremely variable. In the absence of severe carditis the murmur of most significance is the blowing apical systolic murmur of mitral insufficiency. This may often be localized to a very small area over the apex but is usually more widely heard and is often transmitted toward the axilla. Mitral and aortic diastolic murmurs may appear transiently during the period of active carditis and may not in themselves be indicative of valvular disease. Often they reflect relative dilatation of various chambers indicating myocardial weakness. However in some cases of acute rheumatic fever frank aortic insufficiency and rapid progression of mitral disease to stenosis occur.

Definite cardiomegaly develops in a variable percentage of patients with rheumatic fever during the acute phase of the disease and provides reliable evidence of cardiac involvement. The myocarditis that results in a dilatation of the various chambers is also responsible for the occurrence of heart tones of poor quality. This alteration of heart sounds may not be easy to appreciate during the acute phase of the disease but the crispness of tone that returns after subsidence of the myocarditis stands in striking contrast to their mushiness observed during the active disease.

A small percentage of rheumatic children develop a pericardial friction rub at some time during the acute phase of the illness. This manifestation of pericarditis may be quite transitory or may persist for long periods. Because of the intermittent and transitory character of the physical findings pericarditis may be easily missed. Some but by no means all of these patients have electrocardiographic evidence of pericarditis even when the physical findings are absent.

Although cardiac failure is unusual during the first attack of rheumatic fever it is commonly the commanding feature of the disease in those patients with the severe carditis that develops with repeated attacks of rheumatic fever.

From the statistics presented by Jones and others it is evident that overt clinical carditis is the manifestation of greatest prognostic significance in acute rheumatic fever. Severe carditis is responsible for the death of children during the acute phase of the disease and its residuals as well as recurrences are responsible for the demise of many of the children who die in years subsequent to an initial attack of rheumatic fever even in the absence of advanced valvular disease. In the past the occurrence of frank heart disease with marked cardiac dilatation and failure signaled a poor prognosis for long life since as many as 80% of such patients died within a 10 year period following such an episode. Whether or not today with modern treatment and effective prophylaxis against rheumatic disease the prognosis associated with a markedly enlarged heart and congestive heart failure is as grave as it was in the patients studied by Jones *et al* still remains to be determined.

on a statistical basis. It is our present clinical impression that, although the manifestations of marked *cardiac dilatation* and heart failure *still are* ominous signs, the prognosis for longevity signaled by these manifestations during the acute attacks *is better* than it was in the series of patients studied by Jones. The other manifestations of the rheumatic state, though of great diagnostic *importance*, are not the cause of the morbidity and mortality from this disease that *occurs* in later life.

MIGRATORY POLYARTHRITIS

Arthritis occurring at the onset of rheumatic fever is found *in some* 40% of these patients and *during the course* of acute rheumatic fever almost 75% will experience some degree of joint *involvement*. It may occur as the only *major manifestation* of the rheumatic process. As with the other manifestations of rheumatic fever, much variability *in severity* of this *complaint* exists. Joint manifestations vary from vague and often mild pains about several larger joints of the upper and lower *extremities* to exquisitely painful and *tender* joints associated with marked heat, swelling and erythema. *Objective* evidence *of multiple joint* arthritis should be present before this manifestation is included as a major criterion. Quite commonly the joints are *only* painful and swollen. *Monoarticular involvement may* occur *but* more typically the larger joints are involved in a migratory fashion. *Severe* arthritis may be present in the ankle *only to* subside completely after a few days and be *replaced* by successive and equally severe disease of the *knees*, elbows, wrists and shoulders. The knees, *ankles*, elbows and *wrists* are the joints most commonly involved though *involvement of* the hips as well as the smaller joints *does* occur. The duration of arthritis in any one joint *is* generally rather *short and* may last from a few days to a few *weeks*. The entire period of polyarthritis is generally limited *to about* the first month of the disease though in severe cases vague *pains* with occasional erythema and tenderness may persist *for some* time in the absence of frank arthritis.

SUBCUTANEOUS NODULES

These nodules are *found* in a variable percentage of patients *with acute rheumatic* fever (12 to 19%). They *seem to* be more frequent in those *patients* with severe carditis and, though they may appear at any time during the course of *acute rheumatic fever*, most commonly develop after several weeks of illness. They not uncommonly appear during the prolonged *convalescent phase* that follows a severe bout of carditis.

Nodules may be found over any bony prominence *but* are *commonest* over the knuckles, elbows and knees, wrists, occiput, medial border of the *scapula* and the spinous processes of *the thoracic and* lumbar vertebrae. At times they *may* also be found beneath the skin of *the palms* or the plantar aspect of *the foot*. They vary in size from a few millimeters to more than a centimeter in diameter and are best seen by stretching the skin *over* the *bony prominences*. They may be *round* or *slightly* oval and vary *somewhat* in consistency. *They* are usually *firm*, movable and painless. The nodules of acute *rheumatic fever are generally more* evanescent than those of rheumatoid arthritis and persist generally only *for* a period of days or weeks, though *they* do at *times* persist for a period of *months*. *Though* these *nodules* are quite characteristic of rheumatic fever, they are not diagnostic since they are indistinguishable *clinically from those* found in rheumatoid arthritis.

SYDENHAM'S CHOREA

This manifestation of rheumatic *fever* has occasioned among its various aspects the *greatest* amount of *controversy*. For most *students* of the disease, *chorea* constitutes a major manifestation of *the* rheumatic state. The rather extreme *variation* in *the incidence* of chorea in association with rheumatic *fever* reflects, we believe, the *difficulty* in diagnosis *presented* by its *less severe forms*. In our clinic 20% of patients *with chorea* have this as the only clear cut manifestation of rheumatic fever. These *isolated cases of chorea* are, however, *closely* linked to the rheumatic

state by epidemiological and long term studies of the course of acute rheumatic fever It has been shown that while the other manifestations of rheumatic fever appear within a period of weeks following the inciting streptococcal infection chorea most commonly occurs several months later The peak yearly incidence of acute rheumatic fever follows closely the peak incidence of streptococcal infection and in those areas where striking seasonal variation is evident the peak incidence of chorea occurs 1 or 2 months later The evidence presented by Taranta *et al* serves to clarify the relationship between streptococcal infection acute rheumatic fever and chorea They studied patients in which chorea was regularly a very late manifestation of rheumatic fever occurring often after subsidence of the exudative manifestations of rheumatic fever at a time when the sedimentation rate acute phase reactants and even antistreptolysin titer had returned to normal When clinical signs of rheumatic fever have been present chorea often bears this same time relationship Various long term studies have also shown that patients with isolated chorea develop in significant numbers rheumatic heart disease *in the years that follow* In our material the age of onset and the sex distribution differ very slightly from those observed with other manifestations of rheumatic fever

The onset is generally insidious and the early symptoms are often recognized only in retrospect The general clumsiness and the deterioration of speech and handwriting which may occur early are rarely attributed to organic disease until some more violent manifestation makes its appearance The severe contortions that accompany such simple movements as picking up small objects generally bring the parents to the physician Disturbances in gait or the loss of coordinated movements have at times led to consultation with either orthopedist and neurologist or neurosurgeon

The variability in the severity of the symptoms *of chorea may be most remarkable* Some children manifest such mild disease that the diagnosis is easily overlooked by both parent and physician In other children the severity is such that serious bodily injury may result from the violent purposeless movements An attack of chorea may run its entire course without becoming particularly severe or there may be intervals as long as several weeks when the child requires hospitalization in order to prevent injury and maintain an adequate dietary intake The duration of an attack of chorea may be as variable as the severity It may last a period of weeks or may extend for more than a year Periods of increased severity are often interspaced with intervals in which the findings may be quite minimal Most commonly following the institution of prophylactic penicillin therapy to prevent recurrent disease the total duration of the disease is limited to a period of three or four months

ERYTHEMA MARGINATUM

A variety of cutaneous manifestations erythema marginatum erythema multiforme erythema nodosum have been found to occur in association with rheumatic fever but with the exception of erythema marginatum none have real diagnostic significance The latter skin rash occurs in only a small number of *cases and often may be seen only in the* latter part of the acute episode The rash may be quite transitory in some patients but in others will persist for long periods of time Erythema marginatum may occur on several occasions during the acute phase of the disease Erythema nodosum and petechiae may at times be associated with acute rheumatic fever Increased capillary fragility is not uncommon and clinically manifests itself in the petechiae and episodes of epistaxis that may occur

MINOR PHYSICAL FINDINGS

Virtually all patients with acute rheumatic fever will be febrile during the acute phase of the disease This most commonly increases in severity during the first 5 or 6 days of the *disease and then begins to wane The febrile* portion of the acute phase generally lasts no more than 14 days though on occasion it may persist throughout the first month and rarely occur in multiple cycles over several months

This fever is usually abruptly terminated by the use of salicylates

Various other findings such as epistaxis or vague arthralgia are often present though these do not constitute particularly reliable criteria since they may accompany many other diseases It is of interest to note that the exsanguinating hemorrhages that were not an infrequent manifestation a number of years ago no longer are seen with any regularity Such episodes of epistaxis as do occur today are little different in frequency or severity from those occurring in normal children Abdominal pain is not a particularly common manifestation but at times can be so extremely severe as to suggest some acute abdominal catastrophe Since appendicitis may occur in this age group the differential diagnosis is sometimes extremely difficult Appendicitis has also occurred in association with acute rheumatic fever A variety of pulmonary findings may also be present in rheumatic fever ranging from those associated with congestive failure to rheumatic pneumonitis The diagnosis of the latter entity remains one of exclusion

EVIDENCE OF PRECEDING STREPTOCOCCAL INFECTION

Of greatest value among the minor manifestations in establishing the diagnosis of rheumatic fever is demonstration that a streptococcal infection has recently taken place In a number of studies carried out in the armed services and in boys schools in England it has regularly been possible to demonstrate both the infection produced by the streptococcus and the subsequent attack of rheumatic fever as its sequellae

In civilian practice however it is usual for the patient with manifestations of acute rheumatic fever to present with an inconclusive history of recent upper respiratory infections In some instances of course the history will be typical of acute streptococcal sore throat or tonsilitis In other instances the history will be vague or the patient or his parents may deny the existence of recent respiratory disease Certainly at the time of occurrence of the rheumatic manifestations telltale symptoms and signs of acute streptococcal pharyngitis are rarely present Careful bacteriological methods will frequently permit isolation of group A streptococci from the throat at this time This is due to the fact that streptococci are not regularly eliminated from the pharyngeal tissues following subsidence of the acute pharyngeal disease Indeed in some instances group A streptococci persist in the tonsillar tissues for many months following subsidence of streptococcal induced respiratory disease Thus in more than 50% of patients who present with manifestations of acute rheumatic fever who have not been treated with penicillin or other antibiotic group A streptococci can be isolated from the throat and provide evidence of the preceding streptococcal disease More uniform and consequently more useful evidence of preceding streptococcal infection can be derived from immunological studies The streptococci of group A which cause acute rheumatic fever produce numerous cellular and extracellular substances a number of which have antigenic properties Consequently evidence of preceding streptococcal infection may be obtained by measurement of an imune response to one or more of these components or products of the group A streptococci For example 80 to 90% of patients developing acute rheumatic fever will have elevated antistreptolysin O titers and at least 75 to 80% will show a rising titer against this antigen (streptolysin O)

This frequency of elevated and rising ASO titers compares favorably with the incidence of elevated or rising ASO titers which follow proved streptococcal disease such as scarlet fever If one seeks evidence of immune response to a battery of streptococcal antigens one can demonstrate evidence of preceding streptococcal infection in the great majority (98 to 99%) of patients in a civilian population presenting with typical exudative manifestations of acute rheumatic fever Thus the association of group A streptococcal disease with acute rheumatic fever is intimate and serves as a substantial minor manifestation in cases where diagnosis is in question

GENERAL LABORATORY FINDINGS

A number of laboratory abnormalities may be detected in acute rheumatic fever. These changes may be extremely helpful in diagnosis and management of rheumatic fever, but nearly as often are a source of confusion to the practitioner. The most consistent of these are the abnormalities in various acute phase phenomena. The erythrocyte sedimentation rate is almost always elevated during periods of rheumatic fever often being as high as 80 to 100 mm. in 60 minutes by the Westergren technique. Indeed, the sedimentation rate is so regularly elevated in acute rheumatic fever that its elevation has been erroneously considered by many to be of diagnostic *significance. It is important to remember* that marked elevation of the sedimentation rate occurs in numerous other conditions and is not of diagnostic significance in acute rheumatic fever. C reactive protein is almost always present in the serum during the acute phase of active rheumatic fever. The latter is a protein not normally present in the blood which appears in the blood during acute episodes of many diseases. Summarized in Table VI are data accumulated in our laboratories which attest both the regular occurrence of this protein in the blood in patients with rheumatic fever and to the lack of specificity of the reaction. The serum mucoproteins have likewise been studied extensively and found to be elevated as a reflection of acute disease in rheumatic fever. In addition to these reactions a variety of other serological phenomena have been found to occur during the acute phase of rheumatic fever. *Though many of these tests were developed* in the hope of finding a specific diagnostic test for rheumatic fever all have proved nonspecific. Similar elevations occur in many other diseases and all of the acute phase phenomena have had their greatest value not as diagnostic aids but rather as indications of the presence or absence of disease activity when the latter is difficult to determine on clinical grounds. The advent of congestive heart failure may produce a dramatic fall in the sedimentation rate whereas this event seems to have no effect on the production or release of C reactive protein or mucoproteins. Consequently, in acute rheumatic carditis associated with heart failure, the C reactive protein or mucoprotein determina

TABLE VI

C REACTIVE PROTEIN DETERMINATIONS IN RHEUMATIC FEVER AND OTHER DISEASES

	Disease	*Cases*	*Positive*	*Negative*
I	Acute			
	Acute rheumatic fever	383	375	8
	Pure Sydenham's chorea	39	5	34
	Convalescent rheumatic fever	175	4	171
	Inactive rheumatic fever	40	0	40
	Erythema marginatum isolated	5	3	2
	Subcutaneous nodules isolated	4	3	1
	Erythema multiforme	10	5	5
	Erythema nodosum	4	3	1
	Rheumatoid arthritis	123	84	39
	Disseminated lupus erythematosus	31	16	15
	Chr. discoid lupus erythematosus	3	0	3
	Periarteritis nodosa	13	12	1
	Dermatomyositis	7	4	3
	Scleroderma	8	5	3
	Pemphigus	18	8	10
II	In Heart Failure			
	Acute rheumatic fever with heart failure	31	31	0
	Chronic active or polycyclic rheumatic fever	9	9	0
	Inactive rheumatic heart disease	19	13	6
	Arteriosclerotic heart disease	18	8	10
	Acute myocardial infarction	13	12	1
	Constrictive pericarditis of unknown etiology	3	3	0
	Subendocardial fibroelastosis	14	2	12
	Idiopathic myocarditis	6	0	6
	Congenital heart disease	16	3	13
III	Congenital Heart Disease Not in Failure	80	3	77

tions may more accurately reflect the acute disease activity than will the sedimentation rate. Treatment with steroid hormones will often rapidly bring the sedimentation rate to normal and result in disappearance of C-reactive protein from the serum even though the subsequent rebound of rheumatic activity which occurs upon cessation of treatment indicates clearly that the attack of rheumatic fever had not completely abated. Under these circumstances the serum mucoprotein concentration seems to provide a better reflection of the duration of active disease than do clinical criteria or either the sedimentation rate or C-reactive protein. Salicylate therapy seems to have no significant effect on the laboratory manifestation of rheumatic fever.

Approximately 70% of patients with acute exudative rheumatic fever have leukocyte counts greater than 12,000 at some time during the first few weeks of disease. However, although long ago recommended as a useful indicator of disease activity, the leukocyte count in our studies has proved singularly unreliable as an indicator of rheumatic disease activity.

The electrocardiographic tracings often but not always are abnormal during the period of active carditis. Perhaps the most reliable and most used electrocardiographic indicator of active carditis is significant prolongation of the P-R interval. In this regard we have found it useful to pay attention only to truly significant prolongation (interval greater than 0.2 second) since minor or borderline prolongations, although of probable physiological significance, are of little clinical usefulness. Abnormalities of rhythm are probably the most common abnormalities revealed by the electrocardiogram and vary from simple sinus tachycardia through abnormalities including prolongation of the P-R interval, reflecting various degrees of atrioventricular block. Auricular fibrilation, though at times present, is rarely observed in association with the first attack of rheumatic fever. A wide variety of electrocardiographic changes may reflect inflammation of the myocardiogram. For example the QRS segment may be broadened, slurred or notched. The QTc interval is frequently increased and much has been made of this change as a delicate reflection of rheumatic carditis. The ST segment may be elevated or lowered reflecting epicardial or endocardial involvement. Repolarization abnormalities may be reflected in alterations in configuration and direction of deflection of the T-waves. An abnormal configuration of the P waves may occur consisting of broadening and notching and increased amplitude. Low voltage of the QRS complex may be found as a reflection of generalized myocardial damage or as a reflection of the damping effect of a pericardial effusion.

MANAGEMENT OF ACUTE RHEUMATIC FEVER

The clinical management of patients with acute rheumatic fever has over the years been the subject of much controversy and confusion. This is due to two facts. *Firstly*, no truly specific therapy is available for this disease largely because the exact nature of the disease is not yet understood. Secondly, because the protean nature of the disease, its great variability and the necessity of extremely long term follow-up studies to evaluate the ultimate effects of therapy on cardiac damage.

At the present time there is no aspect of the management of acute rheumatic fever which is without controversy. For example it has been recently pointed out that the time-honored use of strict bed rest in the treatment of acute rheumatic fever does not have a scientific foundation and is open to question. In our opinion it is only aspects of treatment and prophylaxis related to streptococcal etiology of rheumatic fever which have a firm scientific rationale so these will be dealt with first.

PREVENTION OF INITIAL ATTACKS OF RHEUMATIC FEVER BY THE ADEQUATE TREATMENT OF STREPTOCOCCAL DISEASE

When streptococcal sore throat or scarlet fever are recognized clinically and proved on

ultural grounds the incidence of rheumatic ver as a sequel can be reduced dramati ally by antibiotic therapy adequate to elimi ate group A streptococci from the tissues enicillin is the drug of choice since no linically active strains of group A strepto occi are known which are resistant to this ntibiotic Treatment may be given by the ral or intramuscular route but enough peni illin should be given to provide effective blood levels over a period of approximately 0 days The latter aim may be achieved in number of ways with preparation currently vailable Several acceptable regimens are isted below

(1) Benzathine Penicillin G intramuscu arly in a single dose For children under 1 quare meter surface area an injection con aining 900 000 IU is recommended and for older children and adults 1 200 000 is ade quate to eliminate streptococci from the issues This treatment has many obvious ad vantages including the fact that only a single njection is required The disadvantages in lude the fact that benzathine penicillin in ections are quite painful especially when given to young children and the observations that a high frequency of reactions mostly of a hypersensitivity nature occur following an injection of benzathine penicillin in children

(2) Ten daily injections of procaine peni cillin 400 000 U/day

(3) Three injections of procaine penicillin with aluminum monostearate in oil given at 3 day intervals Children under 1 square meter S A 300 000 U per injection older children and adults 600 000 U per injection

(4) Oral penicillin 250 000 U four times per day for 10 days

Although not as well documented in elim nating group A streptococcal infection as in jections of penicillin erythromycin and the broad spectrum antibiotics such as the tetra cyclines have also been shown to reduce the incidence of initial attacks of rheumatic fever Effective levels should be maintained for ap proximately 10 days

The findings of Cantanzaro *et al* indicate that penicillin treatment begun even as late as 9 days after the onset of group A strepto coccal infection have a striking capacity to prevent their nonsuppurative complications Unfortunately initial attacks and recurrences of rheumatic fever cannot always be prevented by treatment of recognized streptococcal in fection This is due to the fact that strepto coccal infections occurring in atypical form may not be recognized as such but are still capable of inducing rheumatic disease

Since it is clear that virtually all patients who develop rheumatic fever have suffered a recent streptococcal infection for which adequate therapy was not provided we be lieve that all of these patients should be given a full therapeutic course of penicillin This point is of considerable significance since many patients with acute rheumatic disease continue to harbor group A streptococci which can only be demonstrated by intensive cul tural efforts During the acute disease then amounts of penicillin similar to those outlined above for the prevention of initial attacks of rheumatic fever should be given This treat ment will eliminate streptococci from the tissues Treatment with sulfa drugs does not prevent the nonsuppurative sequellae of strep tococcal infection and thus should not be used in treatment of streptococcal disease

Perhaps the most important aspect deriving from the establishment of the relationship of streptococcal infection and rheumatic fever is that it provides the basis for an effective program for the prevention of recurrences of this disease During epidemics of group A streptococcal disease members of the general population so infected develop rheumatic fever in an incidence of 2 to 3% To the contrary numerous studies of rheumatic populations re veal that patients who have had at least one prior attack of rheumatic fever have between 25 and 50% chance of developing recurrence following untreated streptococcal disease Thus the risk of streptococcal infection is in ordinately high in this population compared with the population at large Such figures de mand that every patient who has suffered an attack of acute rheumatic fever be provided with effective prophylaxis against recurrences of streptococcal infection

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It is currently recommended by the Committee on Prevention of Rheumatic Fever of the American Heart Association that all pa

tients who have a well documented history of rheumatic fever or chorea and all patients who show definite evidence of rheumatic heart disease be given continuous prophylaxis against recurrences of streptococcal disease Numerous prophylactic regimens have been utilized and all have been effective in decreasing the frequency of recurrence of this disease The method used in our clinic for all patients where the cooperation of the patient and the parents can be achieved is the administration of oral penicillin 400 000 to 500 000 U/day On this regimen faithfully followed the occurrence of streptococcal infection and recurrences of rheumatic fever are virtually eliminated Toxic reactions are rare and usually of the hypersensitivity type are mild For patients and families who are judged to be less dependable injections of benzathine penicillin in a dosage of 1 200 000 U once each month are given Parenthetically it is fair to point out here that the present Committee on Prevention of Rheumatic Fever and Bacterial Endocarditis of the American Heart Association favors the latter regimen over the former in spite of the pain associated with benzathine penicillin injections and the apparent increase in incidence and severity of the toxic hypersensitivity reactions

Another satisfactory prophylactic regimen is administration of sulfadiazine in a dosage of 0 5 to 1 0 gm per day Toxic reactions to this regimen are likewise rare and usually of little consequence However occasionally leukopenia or agranulocytosis will occur For this reason blood counts should be taken every week during the initial 2 to 3 months of treatment and prophylactic sulfadiazine therapy should be discontinued upon development of urticarial or scarlatiniform rash development of persistent sore throat and when the white blood count falls below 4 000

It is our firm conviction that all patients with rheumatic fever or rheumatic heart disease on hospital wards should be on continuous prophylaxis against group A streptococcal infections

The prevention of attacks of subacute bacterial endocarditis also deserves mention In the past attacks of subacute bacterial endocarditis involving valves damaged by previous rheumatic fever have been a significant problem In many instances these attacks of subacute bacterial endocarditis due in most instances to alpha streptococci have occurred following dental work or elective surgical procedures For this reason it is our current policy to provide all children and adults who have a history of acute rheumatic fever or existing rheumatic valvular disease prophylaxis against this eventuality For this purpose full therapeutic doses of penicillin should be given beginning one day prior to any dental work or operation on the day of the procedure and two days following the procedure

The treatment of acute rheumatic fever as mentioned above, is the subject of the greatest controversy Most students of the disease continue to recommend complete bed rest during acute exudative rheumatic fever in the presence of heart failure or active carditis However, the duration of physical inactivity is being shortened and in the hand of most investigators convalescence appears to be undergoing steady liberalization

In patients with acute rheumatic fever in the absence of overt failure or clinical carditis it is probably adequate to maintain bed rest without restricting toilet or feeding privileges We believe that this regimen should be continued until all evidence of disease activity has abated There then follows a period of gradually increasing physical activity that should be continued for 1 to 2 months depending on the initial severity and the amount of residual heart damage which has occurred Beyond this period we feel the patients should not be restricted beyond the restriction imposed on themselves by their residual cardiac reserve

During the period of fever and arthralgia salicylates can provide remarkable clinical improvement but since they provide only symptomatic relief without altering the fundamental course of the disease, it is necessary only to continue them for this period of the disease On discontinuing salicylate therapy it is not uncommon to note a recrudescence of some of the minor manifestations but these quite uniformly subside within a few days In the past it has often been recommended that salicylate therapy be pushed to the

order of intoxication This it would seem is not necessary or beneficial and satisfactory clinical control can often be achieved with amounts as low as 30 mg per pound in children and six grams a day in adults The aim of therapy with salicylates in our clinic is to control the symptoms of the disease

Of more fundamental importance is the question of whether or not benefit in the eventual outcome in ultimate cardiac function may be derived from the use of cortisone

Extensive controlled studies in which moderate doses of cortisone and ACTH were given over a period of six weeks revealed that in the aggregate the hormones possessed no clear advantages over salicylates and bed rest in the treatment of acute rheumatic fever However relatively recently several studies none of which have been controlled in the strictest sense have again opened the question For example Kelley and his associates insist on the basis of an impressive series of patients treated early in their disease that either ACTH or cortisone in sufficient dosage prevents residual cardiac damage Similar claims have been made by Wilson using much smaller doses of the hormone over shorter periods of time Roy and Massell Markowitz and Kutner and Greenman *et al* have also been impressed with the possibility suggested from their data that large amounts of adrenal steroid provided early in the course of the disease can diminish residual cardiac damage in acute rheumatic fever

Though we believe the evidence available at this time is by no means conclusive it is possible that properly used the adrenal steroid hormones may decrease cardiac damage However it does seem conclusive that to be effective in this regard steroid therapy must be given in high doses during the first few weeks of illness Controlled studies are currently being conducted by various investigators that should provide a clearer answer to this question

If steroids are to be used in these patients the hazards of such high doses given over prolonged periods must not be underestimated The Cushingoid changes that occur will be distressing but of even greater importance are the life threatening complications that may be a consequence of such treatment The dosages necessary greatly enhance the risk of bacterial infection and have caused recrudescences of tuberculosis Serious disturbances of water and electrolyte metabolism and other evidences of "metabolic dishevelment may occur even though prophylactic measures are taken to prevent them Gastritis and peptic ulcers occur with surprising frequency especially when the newer analogs of cortisone and hydrocortisone are used

In those children considered to be candidates for steroid therapy we have initially given cortisone in a dosage of 2 to 3 mg per pound of body weight per day This has then been continued until the clinical signs of hypercorticism became evident and then gradually reduced in small decrements over a period of 6 to 12 weeks A variety of steroids are now available which will accomplish the same purpose but their dosage equivalents when compared to cortisone are still not well defined ACTH may be used rather than cortisone in roughly half the amount recommended above The recrudescence of various manifestations appears to be somewhat more common in the period immediately after the withdrawal of these agents than it was with salicylate therapy but such manifestations can be minimized by the use of a program of gradual reduction in dosage Such symptoms as do occur are generally transitory and do not require the reinstitution of cortisone therapy With such dosage levels of steroids various adjuncts must be used in order to minimize the risk of complications Supplemental potassium chloride in amounts of 1 to 4 gm per day will minimize the tendency to sodium retention but as long as amounts as high as 2 mg of cortisone per pound per day are being administered it is also necessary to restrict the dietary intake of sodium A bland diet and the administration of an antacid preparation may reduce the incidence of gastric complications to some extent Some of the newer anticholinergic drugs may also be helpful in reducing the incidence of complicating peptic ulcers The increased incidence of complicating bacterial infection is felt by many to warrant the use

of prophylactic antibiotics We have felt that the penicillin that these children are taking serves to cover this aspect of management

Of the various problems that present during the course of rheumatic fever, congestive failure is probably the most serious We believe that its management should be no different from the regimens recommended in congestive failure of other etiologies It should be remembered that the benefit to be derived from digitalis is by no means as dramatic as it is in other diseases but it probably provides a worthwhile adjunct to therapy Oxygen therapy and diuretics may be helpful in these crises

Chorea presents a problem in management for which there is as yet no satisfactory treatment Sedation with the various longer acting barbiturates seems to us to remain the best form of management The various tranquilizing agents that are currently available do not appear to be of real value nor have the various newer drugs used in Parkinsonism proved to be beneficial Adrenal steroids and ACTH have also been used in the management of these patients but as yet there is no good evidence that they produce a significant alteration in this most variable manifestation

Finally, the necessity for a lifetime of prophylactic medication, to prevent recurrent streptococcal infections with their attendant extremely high recurrence rate, requires re emphasis This is the only means available to us today by which we may prevent the recurrences of rheumatic fever that invariably result in the extremes of cardiac disability with which we are so often faced today It is this same inordinately high incidence of recurrent infection and repeated bouts of acute rheumatic fever that makes it impossible accurately to predict the outcome for any group of patients There are available in the works of Jones and others the statistics that permit prediction of the course of those individuals that are not prevented, by penicillin prophylaxis, from suffering repeated bouts of rheumatic fever In the years before such a program became available, the prognosis even in the mildest cases of rheumatic fever might be a most gloomy one It is hoped that in the years to come satisfactory statistics will become available from which to predict the outcome of rheumatic fever for those individuals that receive what we now consider optimum management

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CHAPTER 35

Deformities of the Cardiac Valves

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RHEUMATIC fever is the most frequent cause of deformities of the cardiac valves but less than half of the patients with rheumatic heart disease have a clear history of an attack of rheumatic fever Until the last few years it made little difference to the patient whether an exact diagnosis of the type of structural heart disease was achieved Only symptomatic treatment was possible

Indeed the effort that used to be spent in training physicians to recognize the types of heart disease is amazing since the information had so little practical application The first successful operation for valve disease provided a vivid justification for this effort since internists were actually prepared to choose patients that could be benefited by operation We know that correct diagnosis is necessary to permit advances in operative techniques for success in cardiac surgery closely parallels the accuracy of preoperative diagnosis An incorrect diagnosis may lead to an awkward surgical approach that will cause failure

Cardiac catheterization and angiocardiography have great value in the diagnosis of congenital heart disease The physical examination is the most important element in the diagnosis of acquired valvular disease and in the selection of patients for operation However the clinician s success has been substantially aided by clinical physiologists who defined the pathologic physiology of rheumatic heart disease In fact success in the surgical treatment of heart disease is greatest when the clinician the physiologist the radiologist and the surgeon have the closest liaison The efficacy of the team effort in the treatment of human disease is illustrated best in this sphere of medicine

Though surgical treatment of rheumatic valvular disease is a very exciting medical event in this era of rapid medical progress prevention of rheumatic fever with repeated bouts of carditis is still the primary aim[1] in the control of this disease

PATHOLOGY

Rheumatic heart disease affects all cardiac structures the valves endocardium cords and muscle Healing of rheumatic lesions produces the serious structural change in the valves affecting singly or together the cordae tendinae the valve rings and the leaflets

The Aschoff nodule is the typical lesion of rheumatic carditis In it many round cells surround a zone of central necrosis A few giant cells are scattered through the lesion The perivascular location is the usual one but it may vary Usually it remains near a small vessel In many areas the lesion is accompanied by changes in the staining properties of the ground substance of the connective tissue

Disease of the valve leaflets results in nodule formation on the edges Similar lesions occur on the tendinous cords Healing may result in deformities of the valve ring the leaflet itself or the cordae tendinae Calcification of the valve may be a later stage of the healing process These deformities produce the clinical symptoms and signs of valvular heart disease

over the conus area immediately to the left of the sternum in the third and fourth interspaces. Overactivity here means the right ventricle is working against increased pressure in the pulmonary circuit. Sometimes this activity can be so great that movement of the chest wall will be reflected to the apical area and cause confusion as to the site of origin. Under these circumstances if one places the right hand over the apex and the left over the conus one can detect a normal apical beat. It precedes the abnormal impact felt with the left hand over the conus. This is evidence for selective enlargement of the right ventricle.

In order to make a diagnosis of mitral stenosis, the auscultatory findings must be present or accounted for in addition to the findings of palpation and percussion. But without the help of these ancillary physical signs, the auscultatory findings may be misleading. For instance in aortic insufficiency, a diastolic murmur (Austin Flint murmur) may be heard at the apex in the absence of structural mitral stenosis.

Blood flows from the left auricle into the left ventricle during diastole because of the pressure differential. Blood flow through the stenotic mitral valve produces a rumbling mid diastolic murmur. As long as the rhythm is normal contraction of the left auricle forces a sudden squirt of blood into the left ventricle just before the onset of ventricular contraction. This causes the presystolic murmur of mitral stenosis. If the atria are fibrillating the presystolic murmur is not present. With severe obstruction at the mitral valve, pressure in the left auricle and pulmonary circuit remains higher than normal throughout the cardiac cycle. Especially during systole, the pressure in the right ventricle may rise far above normal. The high pressure in the pulmonary artery closes the semilunar valves with a loud snap. This loud snapping second pulmonary sound is evidence of increased pulmonary arterial pressure. It is also an essential finding in mitral stenosis.

When blood flows from the left auricle to the left ventricle, the normal mitral valve opens widely and there is minimal movement of the valve ring. In severe mitral stenosis, the stenotic valve, which has been pushed back into the left auricle[3] by the intraventricular pressure during systole, is rapidly invaginated with a snap into the ventricle by the increased pressure in the left auricle. This is the opening snap of the mitral valve and is characteristic of tight mitral stenosis. Shortly after the snap and associated with systolic contraction of the left ventricle, there is an increase in intraventricular pressure which pushes the mitral valve membrane back into the left auricle with consequent accentuation of the first heart sound.

There is no one place on the chest wall of all patients where these sounds can always be heard best. On the other hand, they may be heard clearly at certain points in any one patient and actually may be inaudible in adjacent regions.

The middiastolic rumble and presystolic murmurs usually are heard best in the fourth or fifth interspace slightly lateral to the apex beat. Occasionally, they may be heard medial to the midclavicular line. Diastolic murmurs of mitral stenosis may be accentuated by increasing the heart rate with mild exercise and by placing the patient in the left decubitus position. Sometimes it is helpful to listen while the patient holds his breath in expiration.

Often the murmurs of mitral stenosis are extremely difficult to find and in a cursory examination may be missed. Herein lies the greatest importance in palpation and percussion because one finds hints of abnormality of the heart. A careful search may then detect characteristic auscultatory signs of valvular disease.

DIAGNOSIS

One of the most difficult problems in evaluating patients with mitral disease for surgery is to determine the predominant mitral lesion. Some mitral insufficiency is usually associated with mitral stenosis. The question is how much. The fluoroscopic findings of enlargement of the left auricle and right ventricle indicate mitral stenosis. Left ventricular enlargement instead of right indicates mitral insufficiency. The electrocardiogram may

disclose left ventricular hypertrophy to substantiate the signs detected on physical and fluoroscopic examination

Measuring the wedge pressure by cardiac catheterization will not make this differentiation in cases where the diagnosis is uncertain by physical, x ray, and fluoroscopic examination In certain patients, exploratory thoracotomy and palpation of the mitral valve through the auricle may be necessary before one is certain which lesion predominates

The ordinary treatment for congestive heart failure will usually improve failure caused by mitral stenosis Dietary salt restriction and mercurial diuretics are particularly helpful The effectiveness of digitalis cannot be predicted without trial but often it is helpful Restitution of auricular fibrillation to a normal rhythm' may increase pulmonary symptoms

Bronchospasm and allied asthmatic symptoms should be treated with intravenous or rectal aminophylline If infection of the bronchial tree is a factor, antibiotics may be used Occasionally phlebotomy will produce temporary improvement On the other hand if massive pulmonary hemorrhage is a factor, transfusion of packed erythrocytes is indicated

Finger fracture of the stenotic mitral valve may be strikingly successful in many patients Success of the operation does not yet indicate that it should be done on patients who are asymptomatic and have only the physical findings of mitral stenosis Symptoms should be present and progressive before operation is performed Other indications for operation are the onset of cardiac arrhythmia or the occurrence of emboli

Patients with severe aortic valve disease in addition to mitral stenosis are apt to be worse after successful fracture of the mitral valve Consideration[6] should be given to dilation of a stenotic aortic valve at the same operation Finger fracture of the tricuspid valve may be successfully done at the time of mitral operation Active rheumatic carditis and bacterial endocarditis are contraindications to operation

AORTIC INSUFFICIENCY

Rheumatic fever is the commonest cause of insufficiency of the aortic valve Congenital defects of the leaflets may also interfere with normal action of the valve Syphilis leaves the leaflets intact but insufficiency is produced by dilatation of the valve ring at the root of the aorta Apposition of the leaflet margins is no longer possible

PHYSIOLOGY

A leak in the aortic valves permits regurgitation of blood into the left ventricle during diastole There is no obstruction to outflow The left ventricle dilates and hypertrophies to compensate for regurgitation of blood The stroke volume increases The heart rate increases slightly to help maintain an adequate flow of blood to the periphery Peripheral signs depend on the hemodynamic changes of increased pulse pressure and lowered diastolic pressure The net cardiac output is reduced

SYMPTOMS AND SIGNS

The symptoms of aortic insufficiency are limited until cardiac failure supervenes Palpitation may be disturbing even at rest Exaggerated pulsations in the carotid artery produce the characteristic bobbing of the head with each systole Segal *et al*[7] emphasize the frequency of angina pectoris associated with free aortic insufficiency It occurred in 38% of their patients They also found the disease was asymptomatic for an average 10 3 years Congestive failure was present for an average of 6 6 years although the range was from 2 months to 30 years The symptoms of aortic insufficiency are the usual ones of congestive heart failure The signs, on the other hand, are more characteristic

Left ventricular overactivity clearly suggests the anatomic lesion The aortic valve opens widely with systole and quick ejection

from the ventricle follows There is considerable back flow for which the ventricle must compensate by more work This causes increased precordial activity The rate is normal or increased and there is no sensation of heaving or straining elicited by palpation of the precordium The sensation is one of quick action and contrasts markedly with aortic stenosis The apical beat is usually found in the sixth interspace rather than the fifth If the valvular lesion is functionally significant the pulse pressure is widened causing a celer pulse Corrigan's pulse Duroziez's sign capillary pulsation and the pistol shot sign may or may not be present Their presence depends on the extent of the hemodynamic derangement

The characteristic murmur of aortic regurgitation is a high pitched blowing diastolic murmur easily obscured by other noises It is heard best with the diaphragm of the stethoscope on a line beginning in the aortic area crossing the sternum and turning downward along the left sternal border The point of greatest intensity along this line varies from patient to patient When ancillary signs suggest aortic insufficiency thorough search may detect a diastolic murmur which is easily missed The patient should lean forward and hold his breath in expiration while the examiner listens Occasionally the murmur may be heard only with the patient on his hands and knees These maneuvers increase the intensity by moving the heart closer to the anterior chest wall

The increased flow of blood from the left auricle into the left ventricle may produce a mitral diastolic murmur in the presence of a normal mitral valve This is the Austin Flint murmur When combined aortic stenosis and insufficiency occur proper interpretation of the physiologic changes in the circulation helps determine which lesion is significant

TREATMENT

The usual treatment for congestive heart failure is singularly ineffective in the control of failure caused by aortic regurgitation Digitalis diuretics restriction of activities and salt in the diet may provide some respite in early failure but usually deterioration proceeds rapidly after the initial break in compensation

The Hufnagle valve placed in the descending aorta aids blood flow distal to it but its greatest value lies in its suggestion of other mechanisms to be developed The idea[8] of forming an intraaortic flutter valve on the distal end of the transsected aorta is promising because the valve is formed of natural tissue

AORTIC STENOSIS

Rheumatic fever is the most frequent cause of aortic stenosis Congenital defects of the leaflets also hinder blood flow The congenitally deformed bicuspid valve is commonly associated with other congenital defects

PHYSIOLOGY

Stenosis of the aortic valves hinders the flow of blood from the left ventricle into the aorta Hypertrophy of the ventricular muscle occurs as the force of contraction increases to overcome the partial obstruction The systolic effort of the ventricle is prolonged The peak of the systolic blood pressure is reached slowly and sustained The arterial pulse wave is flattened on top and it lasts longer than normal Blood flow in the coronary arteries is interfered with by the prolonged contraction

SYMPTOMS AND SIGNS

The first symptoms of aortic stenosis reflect a decreasing cardiac reserve Excessive or unusual exertion may precede bouts of nocturnal dyspnea Other patients may be bothered more by substernal pain often with anginal radiation Spells of dizziness or unsteadiness are the major complaints of some patients Activities that require stooping and straining seem to aggravate these symptoms

Syncope occurs in some patients Often these complaints precede symptoms of frank congestive failure by years or months In addition to the deaths from uncontrolled congestive failure patients with aortic stenosis are prone to sudden death No explanation for this predelection was uncovered in the study of Kumpe and Bean[9]

Aortic stenosis produces the largest specimens of the left ventricle The hypertrophy ensues because the muscle works against the stenotic aortic valve This produces a characteristic overactivity of the apical beat that may be seen as well as felt In a compensated heart the rate is slow and the precordium characteristically heaves The greatly hypertrophied muscle strains to force blood through the stenotic aortic valve The apical beat is larger and more diffuse than in the aortic regurgitation The point of maximal intensity usually is in the fifth interspace

Estimation of the pulse contour may provide evidence that the lesion is hemodynamically important Palpation over the aortic valve may reveal a systolic thrill The thrill felt at the base may be confirmed by auscultation Any vibration that can be felt produces a fairly loud murmur since auscultation is more sensitive than palpation The systolic murmur of aortic stenosis is a loud rough rasping murmur transmitted to the neck if loud enough

The intensity of the murmur depends on blood flow as well as degree of stenosis When the cardiac output is sufficiently decreased as in congestive failure or shock the systolic murmur may disappear only to return with increase in blood flow Mitral stenosis may mask the signs of aortic stenosis for the same reason and they may become obvious only after finger fracture of the mitral valve Muffling or absence of the aortic closure sound is a much neglected sign of aortic stenosis though a second sound at the aortic area may be heard in aortic stenosis One explanation is that the sound of the pulmonic valve closure is transmitted to the aortic area

In the recent past certain misconceptions abetted failure of the clinical diagnosis of aortic stenosis One error was to expect a narrow pulse pressure Another was to avoid the diagnosis in the presence of hypertension The blood pressure in aortic stenosis may vary from normal to marked hypertensive levels Rigid insistence on the triad of systolic thrill and absence of the second aortic sound as well as systolic murmur will cause the clinical diagnosis of aortic stenosis to be missed frequently On the other hand to diagnose aortic stenosis every time a systolic murmur is heard will also result in errors Usually corroborative evidence is present to aid in interpretation of systolic murmurs It must be sought The contour of the radial pulse may be altered if the lesion is hemodynamically significant Calcium found in the aortic valve examined fluoroscopically strongly supports the diagnosis

TREATMENT

Conscientious restriction of activity provides the most effective relief from the early symptoms of aortic stenosis Less demand on a heart unable to respond normally will prevent some attacks of faintness and forestall the onset of frank failure

Congestive failure is treated in the usual way but the response may be poor If symptoms are progressive and steady deterioration is evident dilatation of the aortic valve may be done Caution must be used in advocating this operation because fatal aortic regurgitation may be substituted for aortic stenosis

Lesions of the Pulmonary Valve

Stenosis of the pulmonary valve is discussed in the section on congenital lesions of the heart Rarely is the lesion acquired

Non surgical pulmonic regurgitation has been reported infrequently in man Congenital abnormalities of valve cusps rheumatic fever syphilis bacterial endocarditis and trauma to the chest are causes of pulmonic regurgitation Functional pulmonic insufficiency frequently accompanies rheumatic disease of the mitral valve especially mitral stenosis

The symptoms of pulmonic regurgitation are not clearly defined because few patients

have isolated lesions If the regurgitation is hemodynamically significant, overactivity of the right ventricle is produced A soft blowing diastolic murmur may be heard in the pulmonic area

The diagnosis of the organic lesion may be substantiated by data[10] from cardiac catheterization The pulmonary arterial diastolic pressure is low and little different from the right ventricular diastolic pressure There is also a steep slope of the catacrotic limb of the pulmonary pressure curve

[illegible] of the valve [illegible] a Graham Steell murmur. This murmur [illegible]dom has any functional significance, but is important from the clinical aspect Since it is associated with mitral stenosis, it must be differentiated from the diastolic murmur of aortic regurgitation so that patients with mitral stenosis will not be denied operation This can be done by making sure that the physical signs of aortic insufficiency are absent

LESIONS OF THE TRICUSPID VALVE

Stenosis of the tricuspid valve is a rare lesion Ordinarily, this lesion accompanies mitral disease of the stenotic type Hence, the symptoms of tricuspid stenosis are intermingled with those of mitral disease

Presystolic pulsation in the jugular veins may be a helpful diagnostic sign Vessell[11] has amplified this observation by noting the see-saw sensation between two palpating fingers, one feeling the jugular vein and the other the arterial pulse in the episternal notch These signs have limited value because auricular fibrillation is often present

Black and Harkens[6] *emphasize that* tricuspid stenosis diagnosed during life by clinical signs and demonstration of a pressure gradient across the valve by catheter may not be present at autopsy This paradox may be explained by a relative stenosis produced during life when a combination of partial fusion of the cusps and high flow rate may cause functional stenosis Operative relief of mitral stenosis may alleviate this "functional tricuspid stenosis" When tricuspid stenosis is suspected, the right auricle should be explored and the obstruction relieved if present

Tricuspid insufficiency also is associated frequently with long-standing mitral stenosis Occasionally, a systolic murmur may be heard over the tricuspid area The most common and helpful signs are pulsations in the jugular veins and in the liver Jugular pulsations are best found by cranking up the head of the patient's bed slowly until the head of the column of blood in the jugular vein lies at the midpoint of the neck. At this point, regurgitation of blood along the vein may be observed readily and differentiated from transmitted carotid pulsations. The liver should be grasped or pressed between the examiner's two hands to recognize an expansile pulsation Direct palpation with one hand allows confusion with transmitted pulsations from the aorta

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Bacterial Endocarditis

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ONLY 15 years ago, subacute bacterial endocarditis was one of the dread diseases of medicine Spontaneous cures were very rare though often the disease existed for many months before death of the patient occurred After the rules for the use of penicillin were developed in clinical studies, failure of cure because of persistent infection became one of the rare causes of disappointment

Because of improved treatment of this disease, more responsibility falls to the physician to make certain that treatment he directs does not militate against possible success Indiscriminate administration of antibiotics in inadequate amounts to patients who are possible victims of this disease in its early stages may set the stage for failures It always increases the hazard and expense to the patient Therefore, the physician's mandate is stronger now than ever before to be aware of the vagaries of this disease so that it may be recognized and treated promptly

ETIOLOGY

Generally bacterial endocarditis occurs on valves previously damaged by rheumatic fever or an endocardium damaged in some other way A vegetation may occur on the jet area of the ventricular wall opposite a congenital defect or in mural thrombi caused by myocardial infarction Bacterial endocarditis also occurs in patients with congenital cardiac defects, such as interventricular septal defects and bicuspid aortic valves Although infection in a patent ductus arteriosus is not strictly within the heart, it produces a similar clinical picture Extremely virulent organisms occasionally may grow on previously undamaged valves, usually in the presence of cachexia such as that of the last stages of cancer Streptococcus viridans ordinarily accounts for the insidious form while infection with staphylococcus, pneumococcus or other pyogenic organisms usually produces the fulminating clinical disease characteristic of acute bacterial endocarditis

Infection on the valves occurs in 5 to 10% of patients[1] with old rheumatic valvular disease Presumably, fibrin on the abnormal, rough surface of the damaged valve traps circulating organisms This provides a nidus for their multiplication Bacteremia is frequent following tooth extraction and even after mastication when there is an apical abscess Positive blood cultures have been obtained in various studies[1] in 10 to 83% of cases after tooth extraction, depending on the extent of infection and number of teeth removed The exact conditions necessary for the inception of infection are unknown The source of infecting organisms is easier to find Bacteria may gain access to the blood stream from osteomyelitis, furuncles or even pimples, urinary and upper respiratory tract infections as well as from infections of the gums and sinuses Indeed, it is curious that endocardial infection occurs so rarely

Although streptococcus viridans is recognized as the infecting organism in about 80% of the cases, most other pathogenic organisms have been incriminated in one or more isolated case reports Organisms ordinarily not pathogenic have occasionally caused this disease Of 493 cases collected by Blumer,[2] a

streptococcus was found in 70% staphylococcus albus in 9% pneumococcus in 6% and influenza bacillus in 3% The alpha hemolytic strepococcus is the most common agent in all studies These facts are obviously important in treatment Without identification of the organism the clinician has only an 80% chance of choosing effective antibiotic therapy On the other hand if the individual patient is to have the best chance of recovery it is mandatory that every effort be made to identify the causative organism Most viridans streptococci are sensitive 1 0 unit per ml of penicillin but others require a much higher concentration for complete inhibition of growth Enterococci offer a special problem in therapy because they are extremely resistant to penicillin alone but can be eliminated often by penicillin in combination with streptomycin

PATHOLOGY

Virulent organisms in the blood stream quickly penetrate into the depths[3] of the damaged valves Rapid destruction of tissue and ulceration of the leaflet occur Thrombotic masses take the form of polypoid vegetations on the defective endocardium The masses contain bacteria which invade in all directions Weakening of the leaflet permits perforation or rupture of the valve Friable vegetations may organize, often they break off They are carried as emboli through the circulation to lodge in an artery when it is too small to permit further progress

Because of antibodies rarely do emboli cause pyogenic infections where they lodge although mycotic aneurysms result from weakening of arterial walls when emboli lodge in the vasa vasorum or on defective endothelium Focal nephritis occurs when they lodge in the kidneys Rarely a large embolus will plug a renal artery The medium sized arteries of the extremities and abdomen may be occluded by an embolus These complications may be catastrophic More often insidious changes occur in the kidneys and the myocardium With more protracted disease glomerulonephritis occurs The heart muscle is effected in a manner which is much like that of rheumatic myocarditis These two complications account for many therapeutic failures Pulmonary infarction occurs when vegetations on valves in the right ventricle break off Occasionally a paradoxical embolus may occur through a patent foramen ovale Emboli of pyogenic organisms may result in meningitis osteomyelitis and suppuration in the skin Healing of ulcerative lesions on the valves is slow and occurs by fibrosis with subsequent extension of the endothelium to cover the endocardial surface Patchy calcification may occur later

SYMPTOMS AND SIGNS

As in the diagnosis of any disease the *sine qua non* is to think of the disease as a possible explanation for the symptoms and signs Bacterial endocarditis must be considered in all patients with a heart murmur especially if they have fever Many times it is easily eliminated as a possibility At other times it may be extremely difficult

Usually this disease has an insidious onset so much so that weeks may elapse before the patient seeks his physician's help By careful search the physician may find evidence of disease The history is nonspecific Easy fatiguability and general malaise are the first symptoms Later occasional night sweats may be noted Fever is not recognized early by the patient but may be discovered by the physician on direct search Rectal temperatures taken every four hours are most helpful After the disease is more advanced the characteristic diagnostic findings appear

The generalized illness produces anorexia and some weight loss A daily elevation of temperature occurs and sometimes is accompanied by mild headache With increasing tempo chills generalized muscular aches and

arthralgia appear. Embolic symptoms and signs[1] occur. The patient may notice tenderness of a finger pad. On inspection, a small red purplish tender lesion is seen. This is an Osler's nodule caused by a small embolus lodged in a terminal arteriole. Red macular and nodular lesions called Janeway's lesions may appear on the palms and soles. Linear splinter-like hemorrhages[2] may be found under the nails, and their counterpart may be seen in the optic fundi. Petechial hemorrhages are found most easily in the conjunctivae but also occur over the neck, anterior chest and buccal membranes. These lesions may result from emboli but an unidentified component of vascular weakness also is involved at times in their pathogenesis.

Emboli lodging in larger arteries produce characteristic patterns of symptoms depending on the site of entrapment. Infarction of the kidneys is fairly common. Sudden pain in a flank usually heralds renal infarction. Intravenous pyelograms fail to visualize the ischemic kidney if the whole artery is plugged. When the pain is left sided, splenic infarction is a possibility. Pain on movement of the trunk or in breathing are helpful differential points. A friction rub over the spleen may be heard. It must be sought frequently since it is usually transient. Occasionally, infarction of the gut occurs, and this requires prompt resection. Hemiplegia may be the first sign of bacterial endocarditis but occlusion of a vessel of the extremities is more common. Signs of meningeal irritation occur with smaller emboli.

Changes in dermal pigmentation such as the cafe au lait color of chronic illness occur in subacute bacterial endocarditis. The dirty shade of brown is seen on the forehead, chest and neck. Splenomegaly is a prominent finding in the disease. The spleen is two to four times normal size but is rarely huge. Clubbing of the fingers occurs when the disease exists for a long time. Arthralgia and joint effusion are fairly common but swelling and redness are infrequent.

Since bacterial endocarditis occurs most often on damaged endocardium, a heart murmur is nearly always present. The intensity of murmurs depends greatly on blood flow and viscosity as well as on defects of the valvular structures. Only a faint murmur may be heard at times, at others, the murmur may be striking especially if the cardiac output is increased by fever, excitement, or anemia. Changing heart murmurs are overemphasized as a diagnostic sign of subacute bacterial endocarditis. Usually little change in quality or intensity can be noticed from day to day with the patient in a steady physiologic state. On the other hand, the advent of a new murmur or a great increase in the intensity of a murmur from one day to the next, accompanied by signs of worsening congestive failure indicate perforation of a valve or rupture of a tendinous cord. This is strong evidence for the diagnosis of bacterial endocarditis. Slowly developing congestive failure may result from myocarditis plus the underlying valve deformity. When renal failure occurs, it is more often from glomerulonephritis than from focal embolic disease.

DIAGNOSIS

Usually the diagnosis of bacterial endocarditis is easy after it is suspected. Fever, a heart murmur and a positive blood culture provide clear evidence of the disease. Blood cultures are positive in over 80% of cases. If a streptococcus viridans is the causative organism, positive cultures may be obtained from practically all untreated patients. If five cultures[3] are made, at least one will be positive. Partial treatment with even very small amounts of antibiotics make it exceedingly difficult to obtain positive cultures in a reasonable period of time. Bacteria such as brucella organisms are more difficult to recover because of their slow rate of growth in ordinary media. Cultures should be kept for 6 weeks to allow for this if a presumptive diagnosis is made but treatment must not be delayed this long.

In rare patients, recovery of organisms from the blood stream is impossible. Organisms from vegetations in the right heart may be

screened out by the lungs making their recovery difficult No time of day is regularly favorable for obtaining positive cultures nor are cultures taken during high fever positive more often than when the temperature is normal A sufficient number of cultures should be obtained to identify a contaminant Three cultures at intervals during one day and three the following day are usually sufficient Even a small amount of antibiotic in the recent past may require modification of this plan which otherwise is usually successful

From the standpoint both of diagnosis and control of therapy every effort should be made to isolate the organism The culture should be kept in the laboratory until treatment is successful Occasionally only a presumptive diagnosis of bacterial endocarditis must be the basis for treatment if the organism cannot be isolated This situation should be avoided if possible as it is most hazardous for the patient and uncomfortable for the physician particularly when the projected treatment is ineffective

LABORATORY DATA

A normochromic normocytic anemia with 7 to 10 gm of hemoglobin is the rule The mechanism is probably one of accelerated destruction of erythrocytes The white blood cell count may be slightly elevated or may be normal or slightly low Monocytes are usually increased Frequently the urine shows intermittently abnormal numbers of red cells Albumin is found if nephritis is present Azotemia occurs when the nephritis is severe The sedimentation rate is at least moderately increased Serum globulins are somewhat increased in the well developed disease

TREATMENT

Treatment may be divided into three phases the prevention of the disease the specific treatment and supportive measures In the last compilation[5] of data from the University Hospitals of the State University of Iowa no cure was observed before 1940 In the next 5 years one cure was credited to sulfonamides alone and another to sulfonamides combined with ligation of a patent ductus In the period 1944–49 75% of patients were cured of their infection Of 15 failures in this antibiotic period only 2 resulted from persistent infection Usually failures occurred because of heart failure uremia or emboli This study illustrates an important principle in the active treatment of the disease *It must be prompt and effective* The longer the infection persists the greater is the chance that the patient will eventually die of myocarditis glomerulonephritis or emboli even though the infection is controlled

Penicillin is the most effective antibiotic for the treatment of this disease because the usual offending organisms are sensitive to it Bactericidal drugs are more effective than mere bacteristatic ones In order for an antibiotic to be bactericidal in vivo it must be able to penetrate the vegetation in order to get at the organisms within Aureomycin chloromycetin and terramycin are unable to penetrate fibrin in contrast penicillin is able to do this Just as almost every known organism has caused bacterial endocarditis so most antibiotics have been effective in cure in one instance or another This emphasizes the tremendous importance of a bacteriologic diagnosis Knowledge of the in vitro sensitivity of the organism to commonly used antibiotics may be useful even though in vivo the correlation may not be close

In the usual case caused by streptococcus viridans the administration of 4 million units of aqueous penicillin intramuscularly in six divided doses daily is sufficient Treatment continued for 6 weeks will give the highest cure rate Many other plans[6] employing lower doses for shorter periods have been less successful Although penicillin in aqueous solution is rapidly excreted when given intramuscularly every three to four hours this

method of treatment permits high concentrations at frequent intervals This is important in getting the agent into the vegetation in bactericidal concentrations Longer acting preparations of penicillin are less effective are more painful and cause more troublesome reactions The size of the dose must be regulated by the clinical progress of the patient Usually definite improvement in the clinical course can be seen in 3 to 5 days The patient feels better and eats more The fever subsides Occasionally distinct improvement will be delayed until the seventh or eighth days If apparent improvement has not occurred by the ninth day the dose of penicillin should be doubled or tripled In a few cases penicillin in doses of 50 to 100 million units per day has been necessary to control the infection Of course if the organism is an enterococcus streptomycin should be included[7] from the beginning or as soon as the organism is identified Other antibiotics or combinations of antibiotics may be used depending on the causative organism Erythromycin is effective against susceptible organisms and may be given intramuscularly if necessary Anticoagulants have no place in the treatment It is not necessary to use Benemid to obtain high blood levels of penicillin

Treatment should not be started until the physician is certain enough of the diagnosis to commit the patient to the complete program of therapy with its dangers discomfort and expense Just when and under what circumstances treatment should be started with only a presumptive diagnosis cannot be stated succinctly Certainly the chance of cure is lessened by delay Sometimes it is necessary to obtain blood cultures and begin treatment before the organism has been identified After beginning treatment with only a presumptive diagnosis of bacterial endocarditis the full program of therapy is irrevocably committed The course of the disease is modified so greatly by partial treatment that fatal harm may result if treatment is discontinued because of the vacillation of the physician Acting on these principles is most helpful in the difficult case and should increase the chances for success

Another aspect of active treatment and prevention of recurrence is to eradicate sites of chronic infection during the time the endocarditis is being treated After three to four weeks of antibiotic treatment the teeth should be examined carefully for infection Any teeth beyond repair should be extracted We have seen one patient with bacterial endocarditis treated and cured three times within 1 year No further difficulty occurred following adequate treatment of the diseased teeth during the third course of antibiotic therapy

If congestive heart failure occurs it should be managed with the usual measures Arrythmias are no special problem The "small repeated blood transfusions" of yesteryear have no known useful purpose Rest in bed should be continued only as long as the infection is debilitating or congestive failure is a problem Emboli may create special problems which should be treated individually

Care of injection sites is of primary importance for the comfort of the patient The sites of injection should be rotated to reduce pain and induration Both moist and dry heat may be applied to the buttocks Most patients are happy to do this themselves when the materials are placed conveniently at the bedside Injection into the muscles other than the gluteal muscles is especially painful With good care injections into the gluteal muscles may be given every 4 hours for 6 weeks without undue pain abscess or even induration To accomplish this the physician must inspect the buttocks every day and insist on proper care Rarely is it necessary to resort to intravenous administration of penicillin in order to rest the gluteal muscles

Prompt control of infection in a patient with a valvular lesion should prevent the disease Good dental hygiene will prevent many instances of the disease Penicillin or other antibiotics should be given two days before dental extraction and continued until infection is controlled usually 3 to 5 days Prophylactic therapy should be given for lacerations of the skin during obstetrical delivery urologic instrumentation and surgical operations The patient with a valve lesion must know about this disease so that he may warn any physician or dentist he may consult that he has been

a lvised to h ıve prophyl ctic ınt b ot c therapy for ıny oper ıt ve proced re

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CHAPTER 37

Diseases of the Pericardium

RAYMOND F SHEETS, M D

DISEASE of the pericardium is hard to detect because the signposts of malfunction are so few Not many indications of disease are possible in an organ of such simple anatomy and function Pain, when it occurs, does not readily suggest that the pericardium is the site of malady Only an ephemeral friction rub and *the syndrome of cardiac compression* or tamponade strongly incriminate the pericardium

ACUTE FIBRINOUS PERICARDITIS

The symptoms[1] of pericarditis are seldom severe enough to allow clinical diagnosis although asymptomatic forms are probably more common The clinical diagnosis of pericarditis may be easily missed because the pathognomonic clinical sign is so transient *The friction rub of myocardial infarction must* be sought avidly to be detected In uremia and malignant invasion of the pericardium, the signs of the disease may persist longer

Antibiotics and chemotherapy have changed the frequency of pyogenic and tuberculous pericarditis In the past, pneumococci often caused acute disease and often led to purulent pericarditis With the apparently increasing incidence of lupus erythematosus, pericarditis in this disease will be recognized more often Mycotic and parasitic invasion of the pericardium, although rare, is seen Of course, pericarditis occurs in an unpredictable but significant incidence in acute rheumatic fever

SYMPTOMS AND SIGNS

Accentuation of the symptoms of the primary disease may herald extension to the pericardium Pain although seldom severe is the one symptom that indicates pericardial involvement Uremic pericarditis is not often painful although the anatomic changes may be great Sudden excruciating pain occurs oftener in acute pericarditis of unknown cause Extension of the process to the parietal pericardium and adjacent areas of the pleura cause *mild substernal* sticking pain *Although* this may not be a prominent feature in an acutely ill patient, it may be the only clue to the diagnosis A dry hacking cough may be a complaint especially with extension to the pulmonary structures

The friction rub is the most important diagnostic sign of acute pericarditis It may vary in intensity from a barely audible scratch to a vibration which is easily palpated The rub has a to and fro quality which is characteristic The pericardial friction rub must be avidly sought to be found because it may last only for a brief period during one day Even when effusion is a major part of the pericardial process, a friction rub may remain until the pericardial surfaces are held apart by increasing effusion

When only one component is present, a rub may be *confused with a third heart sound* Sometimes the true nature of a noise will be clear only after repeated examinations The transient nature of the sound is *helpful in*

diagnosis A pericardial friction rub may be accentuated by having the patient lean forward to throw the heart nearer the chest wall Voluntary variation of the respiratory movements may clarify the cause in pleuro pericardial rubs

LABORATORY FINDINGS

The *electrocardiogram provides the only* laboratory abnormality suggestive of this disease The electrocardiographic findings[2] are not diagnostic but may be very helpful when interpreted in the context of the history and physical examination The electrocardiographic[3] changes are caused by spread of the process to the sub-epicardial layer of the myocardium Early in the disease ST segment elevation in Leads I and II aVL and aVF is usual The ST segments will also be elevated *in corresponding chest leads As the disease* progresses the segments return to the isoelectric line and inversion of the T waves may occur Q waves characteristic of dead myocardium do not occur but amplitude of the complexes may be decreased in the presence of a large effusion

TREATMENT

Therapy of the primary disease with antibiotic and chemotherapeutic drugs will prevent the complication of pericarditis in many instances of bacterial infection Prompt treat*ment of pneumococcal pneumonia* has certainly diminished the incidence of complications from this disease Local instillations of bactericidal drugs into the pericardium are unnecessary for control of the infection Surgical drainage of pus in the pericardium is rarely necessary any longer but should be considered in neglected or stubborn cases The course of tuberculous pericarditis has been altered beneficially by treatment with streptomycin, isoniazid and aminosalicylic acid in *adequate doses The role of steroid* therapy in rheumatic pericarditis is still unsettled Long remissions have resulted from steroid therapy in lupus erythematosus there have been failures as well

ACUTE IDIOPATHIC PERICARDITIS

Although this disease[4] is similar to acute fibrinous pericarditis the clinical distinction[5,6] *is sufficient* to warrant discussion This is a disease predominantly of young adults No causative agent has been identified There are characteristics in the clinical picture that suggest that it may be a systemic virus disease The inflammatory process involves both the visceral and parietal pericardium The exudate may be bloody *or serous Increase in* the size of the cardiac silhouette has been caused occasionally by dilatation of the heart instead of by pericardial effusion

SYMPTOMS AND SIGNS

The systemic symptoms indicate that this is an infectious disease Anorexia nausea and vomiting occur in the prodromal stage In some instances symptoms of upper respiratory infections including cough coryza and sore throat precede the onset of pericarditis Moderate fever chills or chilly sensations generalized muscular aches and malaise are frequent Other signs of a generalized infectious process are tachycardia and lymphadenopathy

Pain is a predominant feature[7] of this type of pericarditis The onset of pain may be sudden enough to mimic myocardial infarction On the other hand it may be mild and be described as *substernal aching squeezing* or burning Breathing may aggravate it The pain may be diffuse but the midthorax is the most common site However abdominal pain may be complained of before it shifts to the thorax

The most important diagnostic sign of this disease of course is a friction rub It usually is ephemeral its incidence will be highest when it is persistently sought Ordinarily a rub is heard best between the heart's apex and the sternum The to and fro quality may be accentuated in certain positions The rub

obtained at the operation later. After the pericardium is completely healed and calcified the cause may not be found. Hemopericardium[10] has led to adhesive pericardium and calcification. Stab wounds are an obvious form of injury but blunt trauma may be less dramatic and forgotten by the patient. Acute idiopathic pericarditis and diseases like infectious mononucleosis have been suspected as a cause but their role is unproved.

SYMPTOMS AND SIGNS

Slowly progressing shortness of breath is usually the first symptom of restricted heart action. As the heart fails swelling of the ankles appears and is followed by increase in the size of the abdomen. Orthopnea is not a prominent symptom early. Later distention of the neck veins, persistent ankle edema and ascites are striking. Hepatomegaly is common but splenomegaly may occur if the disease lasts long enough.

Considerable reliance may be placed on systolic retraction of the left thoracic wall or a striking Broadbent's sign when they are present. These signs must not be confused with normal intercostal retraction. A paradoxical pulse may be helpful but not diagnostic. Hypotension and a small pulse pressure are common. Exceptions occur. The pulse rate is usually fast to compensate for small stroke volume.

LABORATORY FINDINGS

Slight albuminuria may be present. The venous pressure in the antecubital space is high and the circulation time prolonged. X-ray examination in the series of Dalton et al[11] showed the heart enlarged in one half the patients. In 60% of patients calcium was found in the pericardium by x-ray, operation or autopsy. Fluoroscopy revealed diminished cardiac pulsations in about three quarters of the patients studied. The electrocardiographic findings are nonspecific in this disease although minor abnormalities may be common. Cardiac catheterization[12,13] shows a decrease in the cardiac output. The pressures in the right atrium and vena cava are increased as is the right ventricular diastolic pressure. Evidence of poor ventricular filling may be found rather than incomplete emptying.

TREATMENT

Surgical resection of the constricting pericardium is the only definitive therapy. Holman and Willett[9] emphasize that this must be extensive in order to free the heart completely. Operation may fail because the diseased myocardium is unable to withstand the added work or pericardium is not resected from critical areas. Repeated operations are necessary on some patients with active tuberculosis.

Digitalis is ineffective before operation but may aid the diseased myocardium after it is freed. Mercurial diuretics and restricted salt consumption may be helpful in preparing the patient for operation. Of course active bacterial infections should be treated with appropriate antibiotics. Operation should be postponed until infection is controlled but sometimes this is not possible because of the progressive deterioration of the patient.

PERICARDIAL EFFUSION

Fluid in the pericardial sac is usually secondary to disease of the pericardium or heart. When the volume of effusion is large cardiac function may be interfered with. Any of the causes of acute fibrinous pericarditis may cause symptomatic pericardial effusion. Rheumatic fever, tuberculous pericarditis, metastatic tumors involving the pericardium and acute idiopathic pericarditis are the most common causes of pericardial effusion. Less common causes are diseases such as myxedema, pernicious anemia and uremia.

The type of fluid may vary from clear straw colored to frankly hemorrhagic or purulent depending on the cause. Hemorrhagic fluid has been observed in acute idiopathic pericarditis as well as secondary to invasive tumor. The specific gravity of purulent exudates is

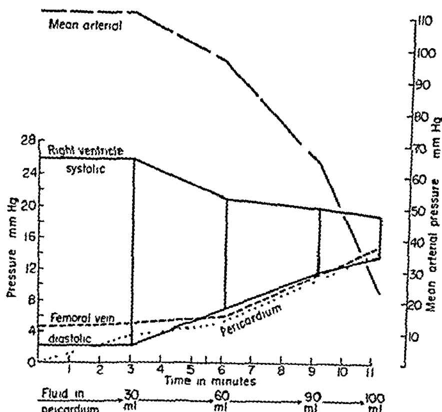


Fig 1 Typical circulatory changes produced by injecting fluid into the pericardium (From Evans, J M, Walter, C W, and Hellems, H. K. Alterations in the circulation during cardiac tamponade due to pericardial effusion An experimental study employing cardiac catheterization *Am Heart J*, 39 181, 1950)

greater than 1 017 and contains varying amounts of cells and fibrin Of course, rupture or penetration of the myocardial wall admits frank blood to the pericardium in contrast to hemorrhagic fluid A useful clinical point is to see whether bloody pericardial aspirate clots or not Small volumes of fluid are common in a great many diseases but symptoms occur only in a few The volume of fluid in the pericardium necessary to produce symptoms is variable because three factors are critical in compromising function the elasticity of the pericardium, the speed of accumulation and quantity of fluid A small volume of fluid in a thick unyielding pericardium will cause trouble promptly On the other hand, 1 to 2 liters of fluid may be less disastrous if it develops slowly so that the sac can stretch

The importance of a rapid increase in the volume of fluid in the pericardium in dogs is shown (Fig 1) in the study by Evans, *et al*[14] With increasing pericardial pressure, there is fall of mean arterial and right ventricular systolic pressure and an increase in femoral vein and diastolic pressures

The critical hemodynamic fault[15] caused by excessive pericardial fluid is the impediment to diastolic filling of the heart The peripheral venous pressure increases because blood cannot flow freely into the right side of the heart With hindrance to diastolic filling, the left ventricular stroke volume is diminished enough to prevent an increase in heart rate from maintaining a normal cardiac output A decrease in blood pressure and loss of effective pulse pressure follows the fall in cardiac output The arm to tongue circulation time is prolonged

When a balance is reached between venous, intracardiac, and pericardial pressures, a weak pulse during inspiration may be detected

This is a paradoxical pulse The volume of the pulse and not the rate is the important consideration The exact mechanism of pulsus paradoxicus has not been delineated clearly

Dornhorst *et al*[16] believe they are able to present a truer statement of the mechanism than were Katz and Gauchat[17]

"Normally the inspiratory drop in intrathoracic pressure is equally applied to the left ventricle and pulmonary veins No change in left ventricular effective filling pressures ensues and no material immediate change in filling or ejection Right ventricular effective filling pressure does increase because the systemic veins are largely extrathoracic This increased filling of the right ventricle is without effect on the left When the pericardium is distended the effect is different In that case increased filling of one ventricle will increase the intrapericardial pressure and hence tend to hinder filling of the other With inspiration the intrapericardial pressure starts to fall but does not fall as far as does the intrath [illegible] vent [illegible] left [illegible]

SYMPTOMS AND SIGNS

Pericardial effusion is asymptomatic until cardiac compression impedes the circulation other symptoms must be ascribed to the underlying disease or pericarditis Dyspnea on exertion and even at rest results from low cardiac output Cough will be a symptom if the distended pericardium presses on the trachea or a bronchus Hiccough may be present as well if the phrenic nerve or diaphragm are irritated Distention of the superficial veins of the neck and enlargement of the liver indicate increased venous pressure Evidence of early liver congestion may be obtained by invoking the hepatojugular reflux test

Force of cardiac contraction as estimated by palpation and auscultation is decreased The heart is quiet and the sounds are muffled When the pericardium reaches sufficient size to compress the left lower lobe of the lung bronchial breathing and dullness of this lobe will occur This sign was described by Ewart

X ray findings may be difficult to interpret Nearly a pint of fluid in the pericardium is required to change the cardiac shadow on the x ray Single films may be inconclusive but serial x rays may make changes in cardiac size obvious Shifting fluid in the pericardium may alter the cardiac silhouette when the position of the patient is changed from upright to reclining but this sign is not specific Decreased cardiac pulsations may be observed by fluoroscopy and kymographic study of the cardiac shadows

DIAGNOSIS

Signs of congestive heart failure a quiet heart and a paradoxical pulse suggest the diagnosis A pulsus paradoxus should be detected with a blood pressure cuff rather than by palpation of the radial pulse The pressure of the cuff should be adjusted to systolic level where waxing and waning of the systolic sounds may be heard in rhythm with respiration

These suggestive findings will lead to a diagnostic pericardial tap when the diagnosis remains in doubt An 18 to 20 gauge needle may be inserted[18] into the pericardial sac either through the fifth interspace just outside the border of dullness or alongside the ensiform process If fluid is obtained 50 to 100 ml air should be injected with the needle still in place Air in the pericardium as shown by x ray makes the source of the fluid quite certain

The danger of pericardial tap is kept at a minimum if the operator does not poke around looking for fluid If a significant quantity of fluid is present ordinarily it is easy to find It may be necessary to briefly and gently touch the heart with the tip of the needle to verify the needle s position This should not be done indiscriminately because the coronary vessels can be injured

TREATMENT

Most diseases of the pericardium may cause enough pericardial effusion to hinder cardiac function but unless tamponade occurs therapeutic taps should not be done In rheumatic fever and most other non pyogenic diseases

the effusion will spontaneously subside with general improvement of the patient. On the other hand, pyogenic pericarditis will need open drainage when specific antibiotic therapy is ineffective. When tumor of the pericardium causes the effusion, the surgical construction[11] of an opening between the pericardium and pleural cavities will give prolonged relief of tamponade. It should be remembered that removal of small volumes of fluid can give marked relief from tamponade, at least temporarily.

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CHAPTER 38

Myocarditis

Raymond F Sheets M D

The term myocarditis refers to a heterogeneous group of diseases of the myocardium In cluded in this large group is the heart disease clearly associated with a primary infection The relationship of myocarditis to such infectious diseases such as diphtheria bacterial endocarditis scarlet fever Weil s disease and the rickettsial diseases is clear although the exact mechanism is not

Gore and Saphir[1] have clearly described a type of myocardial disease that is associated with nasopharyngitis and tonsillitis Their 35 patients died cardiac deaths At autopsy the hearts were enlarged soft and flabby The histologic lesions varied from localized areas of inflammation to necrosis of muscle fibers Although the cellular response was predominately mononuclear the lesions did not have the perivascular position characteristic of the rheumatic nodule Bacteria were not cultured from the heart muscle

In other diseases for instance amyloidosis muscular dystrophy dermatomyositis and sarcoid the fundamental trouble is far more vague Even in the obvious infectious group there is suspicion that many of the myocardial changes are caused not by invasion of the heart muscle but are secondary changes of unknown pathogenesis

Autopsy studies[4] emphasize the fact that disease of the myocardium is far more common than clinical recognition indicates However the histologic appearance of the lesions while showing a sick myocardium are impossible to classify because of similarities of the pictures in varied diseases

The histologic changes[2] produced in the heart muscles of animals on low potassium diets are of interest in this connection The hearts of rats on deficient diets are enlarged The muscle fibers are necrotic and the nuclei absent In the early stages many polymorphonuclear leukocytes infiltrate the involved areas later the cellular infiltrate is predominately mononuclear Similar lesions[3] have been produced by large amounts of parenterally injected desoxycorticosterone Although these lesions did not have an infectious origin the histologic picture resembled that described in some cases of so called myocarditis

A study at the Army Institute of Pathology[4] found 1 402 cases of myocarditis were associated with the following conditions scrub typhus epidemic typhus Rocky mountain spotted fever diphtheria subacute bacterial endocarditis rheumatic heart disease meningococcemia scarlet fever Weil s disease relapsing fever syphilis Chagas disease schistosomiasis malaria trichinosis acute encephalitis poliomyelitis infectious mononucleosis measles Guillian Barre syndrome mumps epidemic hepatitis small pox virus pneumonia tuberculosis Boeck s sarcoid coccidioidomycosis blastomycosis actinomycosis torulosis septicemias acute glomerulonephritis acute tonsillitis acute nasopharyngitis cellulitis and wound infections tularemia brucellosis exfoliative dermatitis arsenical reaction sulfonamide hypersensitivity starvation heat stroke carbon monoxide poisoning emetine use and burns

Just how important the myocardial disease is in the clinical course of many of these conditions is unknown Rather striking terminal histologic changes in the myocardium may have had little to do with the course of the primary disease Usually only the cases of myocarditis severe enough to compromise the pumping action of the heart are recognized clinically

SYMPTOMS AND SIGNS

Systemic symptoms such as fever can be ascribed to myocarditis with assurance only if the acute stages of the primary disease have subsided. Likewise weakness and easy fatigability that persist may be caused by myocarditis. Vague substernal discomfort or heaviness may be complained of. Palpitation and dyspnea may be present on slight exertion but orthopnea may be absent even in the presence of cardiac insufficiency.

Tachycardia persisting after the fever has subsided is a useful sign of myocarditis. Very minor exertion such as turning in bed may cause an increase in the pulse rate. Disappearance of the usual sinus arrhythmia is an early sign of myocardial involvement. The heart sounds lose their crisp normal quality. They sound muffled and have a tick-tock rhythm. A diastolic gallop rhythm occurs in more severe disease as does pulsus alternans. Cardiac dilatation may follow earlier signs of a damaged myocardium. Precordial activity is decreased in this type of cardiac disease. The most common sign is a soft systolic murmur at the mitral area that denotes mitral insufficiency. The systolic murmur may vary in intensity with the heart rate and the degree of fever. Anemia will accentuate this type of murmur also. Diastolic murmurs are unusual in myocarditis and their presence should cause suspicion of another process.

Increasing myocardial insufficiency may not present the usual signs of congestive heart failure unless the onset and progression is slow. Sudden failure of the heart to maintain sufficient output may appear as peripheral vascular collapse or shock. This is probably one explanation for deaths that occurred unexpectedly in diphtheritic myocarditis and other types as well. This is in contrast to the late occurrence and relatively slow development of failure in subacute bacterial endocarditis.

Minor abnormalities in the electrocardiogram are common. They consist often of T wave changes and are not diagnostic but are helpful when correlated with the history and physical findings.

DIAGNOSIS

Myocardial involvement can be found more often if its occurrence is anticipated and repeated search is made during the course of the primary disease. The diagnosis of isolated or Fiedler's type of myocarditis is difficult because it depends to a great extent on the absence of other diseases to which the heart disease could be secondary.

Differentiation of a large dilated heart from pericardial effusion can be very difficult. The x-ray findings of the two lesions may appear identical in silhoutte and contractile motion. Paradoxical pulse may be caused by cardiac dilatation as well as by pericardial effusion with tamponade. The right ventricular pressure pattern originally described in tamponade occurs[8] in other diseases impairing myocardial function such as myocarditis, myocardial fibrosis and subendocardial fibroelastosis. If the patient's condition is critical and tamponade remains a possibility, diagnostic pericardial tap may be necessary.

TREATMENT

Treatment is most effective if concentrated on the primary diagnosis. Adequate timely administration of antitoxin will prevent diphtheretic myocarditis. Prevention of myocarditis is an important reason for prompt definitive treatment of subacute bacterial endocarditis.

The symptomatic treatment of a failing myocardium due to an inflammatory cause may fail but should be tried. Rest in bed to ensure minimal cardiac activity is mandatory. Mercurial diuretics along with restriction of salt intake may be most helpful. Salt in the diet should be limited to 1 or 2 gm daily to prevent unnecessary risk of congestive heart failure. If digitalis is ineffective it will be difficult to

recognize an adequate clinical trial because the usual criteria of clinical response to the drug will be absent Cautious administration will lessen the danger of serious poisoning One of the more quickly excreted preparations such as digoxin or lanatoside C will have an advantage in case toxicity results

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CHAPTER 39

Diagnostic Aspects of Congenital Malformations of the Heart in Infants and Small Children

PAUL ADAMS JR M D and JOSEPH JORGENS M D

GENERAL CONSIDERATIONS

This subject has been chosen for discussion because characteristics of heart disease in the very young age have not been stressed extensively in the past decade as much as have the diagnostic findings of older children with congenital malformations of the heart There is evidence to indicate that almost half of the children born with congenital malformations of the heart fail to survive the first year of life if treated only medically [1] It has ordinarily been assumed that the infants dying at an early age have incorrectable types of malformations Recent experience however would make the clinician realize that many infants with potentially curable types of malformation of the heart are succumbing at an early age These include certain patients with large patent ductus arteriosus [4,6] ventricular septal defect [3,5,6] tetralogy of Fallot[6] and particularly coarctation of the aorta when it is complicated with a patent ductus arteriosus and/or ventricular septal defects [8] Based on our experience perhaps one half of the children dying from congenital malformations of the heart under a year of age do have malformations curable by present surgical techniques Therefore this chapter stresses diagnostic features which will aid early recognition of these malform ns so that salvage will be increased and ferential diagnostic features of othe tions occurring in the infant age g are inoperable Children with co formations of the heart may presen symptoms and signs from the classic description when these malformations occur early in life The purpose of this chapter is to point out these usual but non classical features which have been helpful in separating infants with curable defects from those for which no surgical procedure is yet available

The classification of malformations of the heart into cyanotic acyanotic and delayed cyanosis has been the classical approach [9,11] Perhaps a more helpful approach is the physiologic approach suggested by Bing[10] in which malformations are discussed in terms of whether the pulmonary blood flow is the same decreased or increased over systemic flow This classification is helpful in presenting the material particularly since the roentgen signs of diminished normal or increased flow closely correlate with the measured pulmonary blood flow The subjects of this chapter will be discussed in the order of the radiographic adaptation of Bing s classification

Before the discussion of individual malformations are detailed it is appropriate to discuss the importance of the diagnostic tools that is the hist nd physical examination the electro the roentgenogram angiocardio l cardiac catheteriza tion in the o osis

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ample, if the patient shows signs of irretractable heart failure within a week of age, is only mildly cyanotic, and is hypotensive, this infant is most likely suffering from a "non-functioning left ventricle," which may be secondary to aortic atresia, mitral atresia, or premature closure of the foramen ovale.[13] If, however, the patient shows signs of heart failure in the third or fourth week of life, does not appear to be cyanotic in oxygen, and has weaker femoral pulses than radial pulses, then coarctation of the aorta is the most likely diagnosis. If the history of a slow pulse rate in utero or at birth is obtainable, a congenital complete heart block is likely. Probably half of these children have no other associated malformations of the heart and as such represent a reasonably good prognosis.[14,39] Episodes of rapid heart action beginning at birth or shortly thereafter suggest congenital supraventricular tachycardia. These patients often have no associated intracardiac congenital malformations of the heart.[1,23]

The onset of cyanosis in the first few days of life is common in transposition of the great vessels, in pulmonary stenosis of a severe degree, and in pulmonary atresia or tricuspid atresia with patent foramen ovale. In tetralogy of Fallot a latent non-cyanotic period of several months is usual. In fact, almost all of the malformations having increased pulmonary flow and venous-arterial shunts such as a truncus arteriosus, single ventricle, total pulmonary venous return to the right atrium and others usually do not show obvious cyanosis early but merely desaturation when the systemic blood is analyzed for oxygen content.

Inability of the child to gain weight adequately has been a helpful sign indicating the urgency for specific diagnosis and treatment at a young age. As a general rule, the non-cyanotic child who grows at a normal rate and who has a normal sized heart is usually not an urgent diagnostic problem. It seems reasonable to assume that a child with even a simple malformation such as a patent ductus arteriosus or a ventricular septal defect who reaches the weight of 10 lbs. and does not gain for several months thereafter will not live long enough to wait for diagnostic procedures and surgery at the age of 3 to 5 years.

Frequent upper respiratory infections and pneumonias suggest a malformation with increased pulmonary blood flow. It has been our impression that children with decreased or normal pulmonary blood flow have no increased number of respiratory infections.

Many important findings that are indispensable in arriving at the final diagnosis are elicited by simple physical examination.

Frequently heart murmurs are not heard at the newborn examination. More often they are heard at the 6 week check-up or even later. This is in part a reflection of the more nearly balanced pulmonary and systemic resistances and the small cardiac output in the infant. Only a slight murmur may exist in transposition of the great vessels, single ventricle, severe pulmonary stenosis, or pulmonary atresia. Over half of the infants with coarctation of the aorta and endocardial sclerosis who are in difficulty are without a prominent murmur.

The most common murmur indicating congenital heart disease is systolic in time and maximum along the left sternal border.

Murmurs of grade IV or V intensity have been associated with a pulmonary infundibular stenosis and a ventricular septal defect which shunts left to right. If the murmur is systolic in time and maximum in intensity at the apex of the heart, an atrioventricular canal[18] or corrected transposition of the great vessels with mitral insufficiency[17] is strongly suggested.

Patent ductus arteriosus does not usually produce the typical "machinery" murmur below a year of age. This characteristic sign develops in many patients between 12 and 24 months of age. Rarely its appearance is delayed until after age five.

A palpable suprasternal thrill is obtained in aortic stenosis and less frequently in a patent ductus arteriosus, pulmonary stenosis, and coarctation of the aorta.

The blood pressure determination is most helpful in coarctation of the aorta. Here hypertension may be present in the arms and hypotension in the legs.

A strong sharp pulse and a wide pulse pressure is seen in a left to right shunt at the aortic level such as in patent ductus arteriosus, aortic-pulmonic window and truncus arteriosus, congenital ruptured sinus of Valsalva, ventricular

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This subject has been chosen for discussion because characteristics of heart disease in the very young age have not been stressed extensively in the past decade as much as have the diagnostic findings of older children with congenital malformations of the heart. There is evidence to indicate that almost half of the children born with congenital malformations of the heart fail to survive the first year of life if treated only medically.[1] It has ordinarily been assumed that the infants dying at an early age have incorrectable types of malformations. Recent experience, however, would make the clinician realize that many infants with potentially curable types of malformation of the heart are succumbing at an early age. These include certain patients with large patent ductus arteriosus,[4,6] ventricular septal defect,[3,5,6] tetralogy of Fallot[6] and particularly coarctation of the aorta when it is complicated with a patent ductus arteriosus and/or ventricular septal defects.[7,8] Based on our experience, perhaps one half of the children dying from congenital malformations of the heart under a year of age do have malformations curable by present surgical techniques. Therefore, this chapter stresses diagnostic features which will aid early recognition of these malformations so that salvage will be increased and outlines differential diagnostic features of other malformations occurring in the infant age group which are inoperable. Children with common malformations of the heart may present different symptoms and signs from the classic description when these malformations occur early in life. The purpose of this chapter is to point out these usual but nonclassical features which have been helpful in separating infants with curable defects from those for which no surgical procedure is yet available.

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Before the discussion of individual malformations are detailed, it is appropriate to discuss the importance of the diagnostic tools, that is, the history and physical examination, the electrocardiogram, the roentgenogram, angiocardiography and cardiac catheterization in the over-all diagnosis.

In the history the age of the patient, the onset of cyanosis and the development of the child are essential information. The age of the patient is important in diagnosis. For ex



Fig 1 Normal Angiocardiogram In the Left Anterior Oblique View A B and C shows the successive filling of the right atrium, right ventricle pulmonary artery left atrium left ventricle and aorta

diminished pulmonary flow make this diagnosis a highly suspicious one The peaking of P waves especially in lead 2 of the electrocardiogram indicates right auricular dilatation and hypertrophy and may be secondary to pulmonary stenosis or atresia tricuspid stenosis or atresia or right heart failure Notching of the P waves indicates left atrial disease

The x ray findings and fluoroscopic findings are extremely important and will be discussed in more detail under each individual malformation Four roentgen views of the heart the anterior posterior view the left and right anterior oblique and the lateral view are most helpful in this part of the study A barium mixture given orally is an aid in determining the position of the aortic arch and the presence of left atrial enlargement The roentgenogram is more valuable in determining the over-all size of the heart in infants and children than percussion The estimation of the pulmonary blood flow from the roentgen picture of the pulmonary vasculature is extremely important in categorizing the various types of malformations of the heart Normally small infants appear to have less pulmonary vascular markings than the older child with normal cardiovascular physiology

Left atrial enlargement or its absence may have significance when taken in conjunction with other findings For example infants and children with ostium secundum type atrial septal defect rarely show an enlarged left atrium If an enlarged left atrium is seen then an atrio ventricular or ventricular septal defect should be considered Total anomalous pulmonary venous return to the right atrium has no left atrial enlargement[37] Except for the above two mentioned conditions almost all other defects showing evidence of increased pulmonary flow have evidence of left atrial enlargement of some degree in infancy Left atrial enlargement is also seen in the presence of mitral stenosis aortic stenosis and coarctation of the aorta

ANGIOCARDIOGRAPHY AND SELECTIVE ANGIOGRAPHY (FIG 1)

In angiocardiography radio-opaque media is injected into the venous circulation while serial roentgenograms are obtained with a rapid film exchanger This procedure has been of great diagnostic aid especially with the cyanotic infant By following the course and density of this opaque material right to left shunts may be frequently determined and in addition areas of radiolucency represented by dilutions of this opaque material by left to right shunting may be equally important In the small infant the superficial malleolar veins of the ankle or the cephalic vein (allowing the median basilic vein to be saved for possible future catheterization studies) can be injected The patient is placed in the right posterior oblique position This gives the best delineation of the right and left atrium and the left ventricle However if specific malformations are suggested from the clinical evidence and no biplane unit is available other views may be indicated For example in tetralogy of Fallot the demonstration of the outflow tract of the pulmonary artery and right ventricle has been best delineated in a very shallow left posterior oblique position If corrected transposition of the great vessels is suspected the anterior posterior position gives the best view The risk figures for this procedure are hard to evaluate being

septal defect with aortic insufficiency and bicuspid aortic valves. Weak pulses early in life suggest a non-functioning left ventricle or total anomalous pulmonary venous return to the right atrium.

Certain congenital defects in body development are associated with congenital heart disease.

The child who shows cardiomegaly on the roentgenogram and left heart strain on the cardiogram should be examined for absence of deep knee reflexes, scoliosis, pes cavus, since such a combination of findings indicates the presence of Friedreich's ataxia.[18] The finding of peripheral edema early in life with a short webbed neck and other characteristic features suggests a Turner's syndrome[9] and its frequently associated malformation of coarctation of the aorta. The tall thin infant or child with arachnodactyly suggest Marfan's syndrome and its characteristically associated aortic disease or mitral valve anomaly.

The electrocardiogram as an isolated tool seldom, if ever, is pathognomonic of any specific malformation of the heart. However, certain patterns do occur which, taken in conjunction with the history, physical findings and other data, help in confirming a diagnosis.

Normal infants at birth have a right ventricular preponderance which persists for several months of life. The lack of right ventricular activity or the finding of a left axis or left ventricular preponderance and peaked P waves in the face of cyanosis is suggestive of a tricuspid atresia or pulmonary atresia with rudimentary right ventricle. If the heart is small and the lung fields show diminished pulmonary vascular markings, the tricuspid atresia is most likely associated with an intact ventricular septum or an associated sub-pulmonary stenosis. However, if the x-ray shows an enlarged heart, increased pulmonary vascular markings but no obvious cyanosis, then the left ventricular hypertrophy suggests tricuspid atresia and/or rudimentary right ventricle associated with transposition of the great vessels.

The combination of left axis deviation, a prolonged PR interval, a high R wave in AVL and an incomplete right bundle branch block with an apical systolic murmur is strongly suggestive of an atrioventricular canal or ostium primum type of atrial defect. This same pattern has been found in isolated ventricular septal defect,[30] but in this lesion the murmur is heard along the left sternal border. In coarctation of the aorta with early heart failure the electrocardiogram usually shows a right ventricular hypertrophy and not a left ventricular hypertrophy as is so characteristic in the adult. Should a child with the other signs of coarctation of the aorta show left ventricular hypertrophy and strain pattern, the prognosis appears to be somewhat less favorable.[11] This may indicate an association with endocardial fibroelastosis.

Although an incomplete right bundle branch block may be present in a small percentage of normal infants and children,[41] its presence along with the murmur, an enlarged heart and elements of increased pulmonary blood flow is frequently associated with an ostium secundum type of atrial septal defect.[5] As mentioned earlier, the presence of a slow heart rate might often indicate a congenital complete heart block. The prognosis appears to be related to the presence of other congenital malformations of the heart and in the absence of definite evidence of these may be rather favorable. The findings of congenital flutter, fibrillation or supraventricular tachycardia are indications for prompt and energetic medical treatment.[1, 27] If the heart rate and heart failure are controlled, such arrhythmias may spontaneously convert if unassociated with malformations of the heart. The finding of left ventricular hypertrophy and strain pattern as indicated by negative T waves in the left precordial leads suggest the diagnosis of endocardial fibroelastosis, pericarditis, myocarditis, anomalous origin of the right coronary artery, glycogen storage disease or rarely an intracardiac tumor of the left ventricle.[28] Ebstein's malformation of the tricuspid valve seems to be regularly associated with peaking of the P waves and the presence of a complete right bundle branch block.[16] This malformation should be suspected when the ECG shows the Wolff-Parkinson-White phenomenon (short PR interval, slurred R and prolonged QRS complex).[43] Such findings in association with cardiomegaly and normal to

out of the catheter into a left ventricle an interventricular septal defect or a patent ductus may be outlined

The selective injection of an opaque agent into the heart has three advantages over the standard forward angiocardiogram First the contrast agent is delivered undiluted into the heart chamber giving a better visualization of the chamber Secondly a specific site can be outlined without overlapping opaque areas obscuring the field for example the pulmonic stenotic area in pentalogy of Fallot Finally, in spite of a reversing interatrial communication a communication between the right ventricle and the aorta can be defined by injecting the right ventricle

CARDIAC CATHETERIZATION

In the past 8 years over 1 000 catheterizations have been performed in our center The largest group having this procedure is under 1 year of age We believe in doing this study at an early age when the patient s life expectancy seems limited and an operable type defect cannot be completely excluded on clinical grounds For the past 2 years we have not found it necessary to use any type of premedication or anesthesia Although the infant may sometimes cry at the beginning of the procedure most frequently as the study progresses he becomes quiet and often goes to sleep Infants under 1 year are often fastened to a thin H shaped plywood board with elastic bandage around the arms and legs There are advantages in not using anesthesia First the risk of the premedication and anesthesia itself is eliminated Two of the deaths occurring at or shortly following heart catheterization were attributed in large degree to an improper dose of morphine sulfate The second advantage is the fact that if these infants and children are not asleep their clinical status in the darkened room is more easily followed On many occasions when we have been partially through a procedure the infant will go to sleep and become quiet The procedure may be halted and the patient carefully observed to make sure that no untoward reactions are occurring Third we feel that with the patient awake and breathing room air his cardiovascular hemodynamics are generally more stable than if he is in varying degrees of anesthesia It was not an infrequent occurrence to find systemic arterial desaturation in anesthetized infants following heart catheterization This desaturation has been a much less frequent finding since anesthesia is no longer used

Objections to the practice of doing heart catheterization without anesthesia are that the children may frequently cry We have found the use of the common lolly pop helpful Without anesthesia in a few instances a venous spasm has been severe enough to force shortening of the procedure or to cause inability to catheterize the vein at all Minimal handling of the vein and getting the catheter quickly into the heart and various chambers have been our greatest help along this line Pain associated with changing catheters is often related to severe venous spasm Occasionally with venous spasm the catheter is immovable without stripping the vein In one case the catheter lodged in the axilla could not be moved for 45 minutes Following the administration of morphine however the spasm appeared to be relieved Children under 4 years of age should have heart catheterization if an operable type of malformation needing early surgical intervention is suspected After the child reaches 4 or 5 years heart catheterization is indicated as an elective procedure at the patients and parents convenience when any doubt exists of an accurate diagnosis following conventional studies However if the clinical impression points decidedly against surgery for the malformation in the immediate future the cardiac catheterization is often deferred so that it may be performed more closely to the expected time for surgery

It would perhaps be most helpful at this point to discuss briefly some of the pitfalls associated with heart catheterization In the first place heart catheterization is rarely of complete diagnostic certainty unless data obtained in the history and physical examination electrocardiography and x ray are compatible For example a left to right shunt at the pulmonary artery level may be due to a patent ductus arteriosus less frequently to an AP window or truncus arteriosus or a high ventricular septal defect with streaming Clinical



Fig 2 Selective Angiocardiogram in the Anteroposterior View *Transposition of the Great Vessels* In this case the catheter could not be advanced beyond a ventricular chamber with a high pressure The lateral view showed the catheter to be anteriorly placed Contrast agent injected into this ventricular chamber, showed only the aorta arising from this anterior chamber

Fig 3 Selective Angiocardiogram In this *case the catheter could not be advanced beyond* the right ventricle Because the reason for the *obstruction was not apparent, opaque material* was injected revealing a huge medially placed pul*monary artery*

strongly dependent upon the type of patients selected for this procedure It has been our *policy not to deny patients this procedure if* an operable lesion might be demonstrated Out of about 750 angiocardiograms performed during the past 8 years, we have had three deaths These patients had primary pulmo*nary hypertension, severe pulmonary stenosis,* and mongolism with cyanosis and dextrocardia Also during this time about six infants scheduled for angiocardiography the following day did not survive long enough to have that procedure done This procedure has also been used on patients appearing to be in the end *stages who have tolerated it surprisingly well*

When the child is in the age group at which heart *catheterization* can be *performed* through an arm vein, selective angiocardiography is usually the procedure of choice Selective angiocardiography is a term applied to *the injection of a contrast agent through a* catheter into a specific vessel or chamber of *the heart It is suggested as a supplement to* heart catheterization if an angiocardiogram is necessary, or if the chamber in which the catheter is located cannot be named Frequently the catheter cannot be advanced into *the outflow tract of the right ventricle* By injecting contrast agent through the catheter *the position of the outflow tract can be defined* Once this position is located the catheter may be advanced further, or the type of lesion may be apparent (Figs 2 and 3) For example, contrast agent injected into the right ventricle may outline a pulmonary stenosis, a truncus or a transposition of the great vessels If the *contrast agent is injected into the right* atrium and it all passes into the left atrium, a diagnosis of atresia *of the tricuspid valve is strongly* suggested If the contrast medium is ejected

ills of heart catheterization are nu ... and a competent experienced team is ... al for the exact diagnosis of a congenital ... heart

SELECTION OF PATIENTS FOR SURGERY[77]

This topic will be discussed briefly under each paragraph concerning the specific malformation under discussion. General principles applicable to the whole field of cardiovascular surgery may be helpful. The chief duty of the clinician or cardiologist is to determine correctly and accurately the specific operable defect. If the defect is not discovered or during surgery unexpected complications arise which could have been foreseen, the patient is subjected to great and unnecessary risk. If surgery is performed on an inoperable case the same hazards confront us. The mere presence of an operable type of malformation of the heart is in itself rarely sufficient reason for surgery.

In this ever expanding and complex area it has been helpful to me to consider each patient as representing a balance or a gamble in which the patient's over all useful life expectancy is weighed against the risks and gains expected from surgery.

For purposes of generalization, surgery may be grouped into three classifications. First, the "ideal" type of procedure such as the patent ductus arteriosus in which the successful operation returns the heart to normal physiology. The second type is "palliative" such as the Blalock-Taussig extracardiac anastomosis for tetralogy of Fallot in which the patient may be benefited but is left with some residual abnormal physiology. The third and largest category at the present time is the developmental procedure.

Although developmental procedures are tested in the laboratory for reasonable expectancy of success, laboratory conditions are rarely identical to those in the individual human patient. The surgical mortality and the degree of improvement following surgery are unknown. "Developmental surgery has no proven beneficial results to offer and should be performed theoretically only in those instances where life expectancy is obviously poor. We have been constantly amazed by the remarkable recoveries made by the far advanced patients upon the performance of a good developmental curative type of surgery. After a few such experiences it becomes easier for the clinician to recommend a developmental type of curative surgery for patients less seriously afflicted.

A curative type of surgery as a general rule carries the lowest mortality and the greatest hope for beneficial results. When once the basic dysfunction is completely corrected, the patient's chance for recovery is excellent.

Types of malformations for which curative or nearly curative procedures are available include patent ductus arteriosus, coarctation of the aorta, pulmonary valvular stenosis, and some cases of heart tumor. With more experience and final agreement as to the safest method of oxygenation during the bypass, the atrial septal defect, ventricular septal defect and correction of defects associated with tetralogy of Fallot may fall into this category.

MA... ORMATIONS WITH NORMAL PULMONARY FLOW

COARC... ION OF THE AORTA

The signs ... mptoms of this malforma... n of the ... ly occur in older children ... nd its ... known. In brief, many of ... child ... dults are completely with... n ... heart murmur is systolic ... ard over the entire pre... between the scapula... pared to many other ... elevated blood pressure in the arms and unobtainable blood pressure in the legs is characteristic. The electrocardiogram most often shows left ventricular hypertrophy. The x-ray may be characteristic by showing left ventricular enlargement, enlarged aorta and rib notching. The complications result from the hypertension and consist of heart failure, ruptured cerebral vessels. A second common complication is subacute bacterial endocarditis. The probability of a



Fig 4 A Plain film shows anomalous pulmonary vein in the right lung B Catheter was threaded into the anomalous pulmonary vein draining into the right superior vena cava

ECG and x ray findings often clarify the diagnosis The diagnosis is established by passing the catheter through the patent ductus arteriosus or aortic pulmonic window One should remember that the catheter should preferably pass below the diaphragm to be most certain that it is in the aorta On withdrawal from the aorta through the patent ductus and back into the pulmonary artery a definite decrease in oxygen saturation is present in the pulmonary artery If however the catheter went out an anteriorly placed aorta or through a common truncus the oxygen content of the pulmonary sample would be theoretically identical to the sample taken in the femoral artery A left to right shunt at the ventricular level most frequently would be diagnosed as a ventricular septal defect However a very large left to right shunt in the face of balanced and systemic ventricular pressures should make one strongly suspicious of a single ventricle A ruptured sinus of Valsalva into the right ventricle will also give oxygen saturations of high level in the right ventricle In this instance the finding of a lower than expected pulmonary artery pressure compared to clinical symptoms and heart size may be helpful In addition the continuous type murmur heard to the right of the sternum and over the xiphoid process will help at arriving at the correct diagnosis A left to right shunt at the atrial level may be an ostium secundum type of atrial septal defect or an ostium primum atrial septal defect or partial anomalous pulmonary venous drainage (Fig 4) In the ostium primum or AV canal the pulmonary artery pressures are frequently more elevated than in the ostium secundum Helpful signs indicating ostium primum type of ASD is the location of the murmur maximally at the apex rather than in the second and third left interspace, the frequent presence of a thrill and diastolic murmur and the presence of a left axis deviation prolonged PR interval and right ventricular hypertrophy on the electrocardiogram If one finds an extremely high oxygen saturation in the right atrium when slight desaturation exists then simultaneous right atrial and femoral artery samples should be taken to confirm the diagnosis of total anomalous pulmonary venous return

It is important that the exact position of the catheter tip is recognized at the time when pressures are recorded and blood samples are withdrawn to properly interpret the pressure recordings and oxygen saturation values in the blood Frequently it is necessary to turn the patient into a lateral view to ascertain the anterior posterior position of the catheter Errors are made when the catheter is not recognized as being in the great cardiac vein the left lobe of the liver left vertical vein left ventricle or as being through an interatrial septal defect or interventricular septal defect

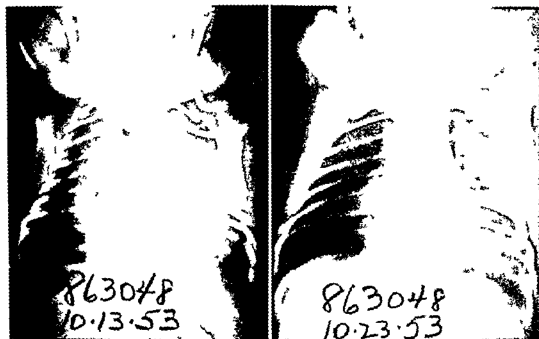


Fig 6 Coarctation of the Aorta in a Male Infant Age 3 Weeks A Radiograph shows non specific massive generalized enlargement of the cardiac silhouette part of which may be due to pericardial effusion B Post-operative film 10 days later

decreasing cardiomegaly and heart failure and will go on to gain weight and compensate for their malformation so that at 6 months to 1 year of age they may frequently be discontinued from such intensive treatment (Fig 8) In the absence of any clinical symptoms or signs an optimum age for excision of the coarctation might be from 4 to 12 years of age but with recurring heart failure or failure to grow one should not hesitate to suggest excision of the coarctation at any age It has been our experience and that of many others that some children with coarctation of the aorta do not respond readily to adequate medical management Some of these children may have an associated patent ductus arteriosus ventricular septal defect or endocardial fibroelastosis However it has been the policy at our center that in the absence of good medical response surgical excision results in a decreased cardiomegaly elimination of heart failure absence of a pressure differential between arms and legs and general clinical well being Although the surgical mortality may be in the neighborhood of 25 to 30 % in such selected patients the mortality would otherwise approximate 100 % If the children surviving this operation live to a near normal life expectancy the results are gratifying

When the patient has a coarctation of the aorta and a patent ductus arteriosus entering the aorta distal to the coarctation (so-called infantile type) the prognosis is generally poorer treated either medically or surgically However should such a patient be tided over medically marked intimal proliferation of the pulmonary arterioles occur Delay in surgery until an older age does not seem advisable We have recently seen a child such as this surviving until nine years of age at which time definitive procedures were undertaken and were not successful[7] It would appear that a reversing patent ductus with coarctation of the aorta is similar in all respects at this stage to a reversing patent ductus arteriosus of an isolated character Surgical excision under six months of age has been successfully accomplished[7 35 4]



Fig 5 Typical Radiograph of Coarctation of the Aorta With a Patent Ductus in a 6 Month Old Male This shows a large left ventricle slightly increased vascular shadows and rounded elevated

less than average life expectancy due to these complications and the adequate results obtained by excision of the coarcted segment have led to the general agreement that when this malformation is diagnosed surgery is indicated as an *elective* procedure at the optimum age of four to twelve even in the absence of symptoms

In this chapter I would like to stress the syndrome of coarctation of the aorta which produces cardiomegaly and heart failure around the first to fifth month of life Accumulated evidence becomes more and more suggestive that perhaps half of the infants with coarctation of the aorta exhibit early heart failure and do not survive *the first 6 months* of life unless treated vigorously with medical therapy or surgical excision of the aortic block[38] If the coarctation of the aorta is uncomplicated by the presence of a patent ductus arteriosus a ventricular septal *defect* or an endocardial fibroelastosis of the left ventricle vigorous medical therapy including digitalis low salt formula and diuretics may sustain these infants for later surgical treatment[7] However a certain number *of infants with coarctation of* the aorta with or without associated malformations do not respond to medical management[7, 8, 38, 39, 51]

A typical history in such an instance is that *the newborn infant is observed to feed poorly* for the first few weeks of life It may be noticed that the eyelids and ankles are edematous The child may be quite dyspneic pale and perspire excessively No heart murmur may be heard A roentgenogram taken at the third or fourth week of life shows massive cardiomegaly (Figs 5 and 6) Blood pressures taken *simultaneously in the arms* and legs will indicate a hypertension usually over *100* systolic in the arms and a significant pressure differential between the arms and the legs If a significant pressure differential is noted *between the arms and legs but the arm* pressure is in the range of 60 to 80 systolic a coarctation with other associated malformations usually exists which make the coarctation inoperable[7, 21]

In case the *diagnosis remains equivocal* following clinical studies a retrograde aortogram is the procedure of choice to outline the coarcted area (Fig 7) A forward angiocardiogram is often not helpful because of poor contrast by the time the opaque material reaches the left side of the heart and aorta

The electrocardiogram will often show only right ventricular hypertrophy The presence of left ventricular hypertrophy or a strain pattern indicated by negative T waves in the left precordial leads may indicate an associated *endocardial fibroelastosis*

Infants with coarctation and heart failure should be treated energetically with *digitalis* If digitoxin is used this should be in the dosage of 0 04 to 0 05 mg per kg as a digitalizing dose and $^1/_{10}$ of this as a maintenance dose A salt free milk formula such as Lonalac should be given *for feedings Mecurial diuretics* in the dosage of $^1/_8$ to $^1/_4$ cc should be used while edema persists Many patients will show

response Others remain free of heart failure but gain no weight during several months of observation In these children surgical aortic valvulotomy under direct vision seems indicated Surgical experience is still too limited to form conclusions as to the ultimate curative value of present techniques

The older child with this malformation may be symptom free but develop cardiomegaly and evidence of left heart strain (negative T waves in the left precordial leads) We have seen sudden unexpected death following exertion in this group Therefore the presence of left heart strain in an asymptomatic patient with aortic stenosis may become the indication for surgical intervention as surgical knowledge and techniques improve



Fig 9 Isolated Aortic Stenosis in a Male Age 4 Months The roentgenogram shows a large left ventricle In this case this lesion cannot be differentiated radiographically from coarctation of the aorta

ENDOCARDIAL FIBROELASTOSIS [6]

This malformation consists of an exceptionally thick endocardium usually confined to the left side of the heart This finding has been found on the right side of the heart associated with lesions increasing the flow and pressure of the right side such as total anomalous pulmonary venous return to the right atrium Some degree of endocardial fibrosis is found in almost all congenital malformations [41] but ordinarily is not a significant complication Its frequent occurrence with aortic stenosis and coarctation of the aorta is well recognized Its presence may affect the operative mortality when such defects are managed surgically

A primary or isolated endocardial fibrosis is thought to be an hereditary trait because of its frequent occurrence with families [47] Whether or not hereditary factors play a significant role in this malformation as compared to other congenital malformations of the heart still requires further study It is well known that endocardial fibrosis may occur without previous history among other siblings

The onset of heart failure may begin at any age usually during the first year of life The great majority of these patients will respond temporarily to medical therapy consisting of digitalis and a low salt formula Their course is gradually downhill and survival beyond a year is infrequent On the other hand some of these children will respond rather dramatically to medical therapy and appear to remain in remission We have followed several of these infants in whom this diagnosis appeared to be reasonably certain who apparently have not become "active" over a period of 5 years In these cases the heart has remained large with left ventricular prominence This is different from the patients showing myocarditis who survive and subsequently have heart sizes which would be considered within normal limits On physical examination these children often appear to be quite pale About half of the children when originally seen do not have significant murmurs and the remainder may have non specific or apical murmurs suggesting myocarditis Unless the infant is in severe heart failure the peripheral pulsations are adequate and blood pressures are within normal limits

The electrocardiogram has been the most helpful in making the clinician suspicious of this defect There is usually high voltage over the precordial leads and particularly the left precordial leads The findings of negative T waves in V_4 V_5 and V_6 of the left precordial leads should make one suspicious of this lesion The roentgenograms and cardiac fluoroscopy reveal an enlarged heart normal vascular markings and a marked left atrial enlargement (Fig 10)



Fig 7 Coarctation of the Aorta in an Infant Retrograde aortogram reveals constriction in distal portion of the arch of the aorta Because of risk this procedure is indicated only when the clinical evidence is conflicting







Fig 8 Coarctation of the Aorta in a Male Infant Age 3 Weeks, A Large left heart B Lateral view shows large left atrium C Under medical management the heart decreased in size

AORTIC STENOSIS

Like many of the congenital malformations of the heart, this defect is ordinarily one which gives very little physiologic alterations early in life so that the patient remains essentially asymptomatic until an older age However, this defect too has a spectrum of severity and some of these children do poorly and die in heart failure at a few months of age

[illegible] f an infant [illegible] failure to [illegible] f signs of cardiac decompensation with dyspnea, pallor, perfuse perspiration and coughing may occur On physical examination the infant is acyanotic and in heart failure with hepatomegaly, pulmonary rales tachycardia A grade three to four systolic murmur is frequently heard following cardiac compensation which was less prominent when first examined A thrill may be palpable The thrill and murmur may be maximum in intensity along the left sternal border rather than the aortic area or in the suprasternal notch as expected classically in the older child

The electrocardiogram will show left ventricular hypertrophy The T waves in V_6 may be negative suggesting the commonly associated fibroelastosis

The roentgenogram shows cardiac enlargement The apex is elevated, the pulmonary artery segment is concave relative to the large heart, the pulmonary vascular markings are normal or congested from heart failure and the left atrium is enlarged on the barium swallow (Fig 9)

These infants may respond to intensive medical management as in some coarctations of the aorta but our experience so far has been discouraging with the long term benefit of medical management since one infant unexpectedly expired following a satisfactory initial

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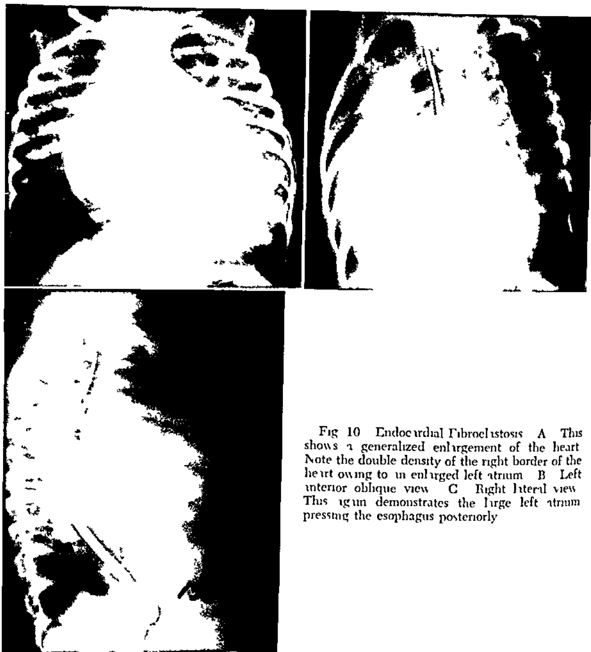


Fig 10 Endocardial Fibroelastosis A This shows a generalized enlargement of the heart Note the double density of the right border of the heart owing to an enlarged left atrium B Left anterior oblique view C Right lateral view This again demonstrates the large left atrium pressing the esophagus posteriorly

The generally accepted treatment for endocardial fibroelastosis at present is the medical treatment for heart failure One surgical procedure which has apparently met with some success has been installation of talcum powder into the pericardium [3] This produces adhesions and increased vascular supply to the myocardium These authors feel anoxia of the myocardium due to obstruction of thebesian vein drainage may be the cause of death in endocardial fibroelastosis The difficulty in evaluating the benefit of this procedure has been the lack of a specific clinical diagnosis short of postmortem examination Another factor confusing the evaluation of such a procedure is the common experience of all cardiologists that some of these children spontaneously appear to develop remissions or become "burnt out" and continue fairly normally for as many years as they have been followed

MYOCARDITIS

Idiopathic myocarditis occurring in the

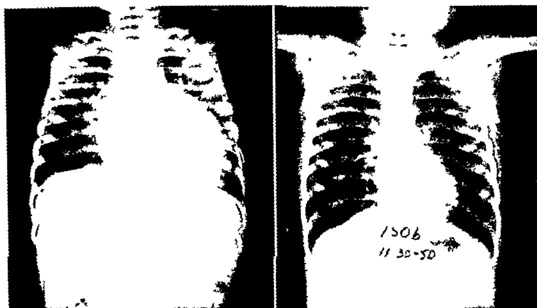


Fig 11 Idiopathic Myocarditis Male Age 5 Years A The cardiac silhouette shows generalized enlargement due either to dilatation of the myocardium or to associated pericardial effusion B Two years later a normal sized heart is seen

young infant has made up the largest proportion of the group of infants with myocarditis We have however occasionally seen the young child about two with myocarditis in which beta hemolytic streptococcus is isolated and presumably the myocarditis is of rheumatic origin Such infants do not show polyarthritis as do older children and adults If a preceding beta hemolytic streptococcal infection and a high value for an antistreptolysin O titer can be established a rheumatic etiology seems justified The rheumatic type of myocarditis under the age of four is unusual however We have seen several instances of typical myocarditis following an episode of measles and chicken pox Since acute glomerulonephritis is associated with myocarditis and some degree of heart failure in a large percentage of infants and children the urine should be examined carefully in each instance The isolation of group A type 12 beta hemolytic streptococcus from the throat is helpful in establishing the diagnosis of acute glomerulonephritis If none of these etiological factors can be implicated the idiopathic myocarditis is assumed to be of viral origin

The history is important in such instances If a previous streptococcal infection or viral contagious disease such as mumps or chicken pox is not found in the history the history then usually consists of gradual listlessness and anorexia Dyspnea and peripheral edema then may appear

On physical examination the findings may include the presence of a diffuse non localized systolic and diastolic murmur most prominent at the apex as in rheumatic myocarditis The heart tones are often of poor quality the rate is fast and arrhythmias may be present

The electrocardiogram may or may not be abnormal Changes in the PR interval indicated by lengthening notching of the P waves and changes in the ST segment and inversion of the T waves are the most frequent changes

The roentgenogram will show an enlarged heart apparently involving all chambers Left atrial enlargement is usual (Fig 11A B) The findings of normal pulmonary vascular markings on the roentgenogram diminishes the likelihood of congenital malformation of the heart producing a left to right shunt or a malformation with diminished flow producing a right to left shunt and cyanosis The finding of normal blood pressures will rule out coarctation

of the aorta Endocardial fibrosis is a difficult diagnosis to separate clinically, but it has been our experience that the voltage in endocardial fibrosis is often high in the electrocardiogram and low in myocarditis

The specific cardiovascular procedures such as angiocardiogram and heart catheterization are not indicated unless questions arise as to the possibility of associated defects

The treatment here as in endocardial fibroelastosis has been medical management At the present time salicylates and hormones are used as in acute rheumatic myocarditis There is general agreement that the use of these drugs are of great benefit in reducing symptoms secondary to the disease Whether or not they alter the ultimate outcome or prevent residual valvular disease has not been conclusively established Since their use may result in severe complications, hormones should be reserved for those instances in which medical management of the more standard variety has not been effective and the patient is showing signs of progressive deterioration

The prognosis for recovery is difficult to evaluate It is obvious that many of these children will progress despite all treatment and succumb to their disease Fortunately, many improve and have been found years later to have normal heart size, no murmurs, or other evidence of cardiac involvement It has been our experience that myocarditis with recovery will ultimately lead to normal roentgen findings whereas endocardial fibroelastosis with recovery leaves a residual cardiomegaly

PERICARDITIS

Purulent pericarditis with effusion secondary to a staphlococcus organism has become a more frequent subject of reporting in the recent literature Death from this complication under 1 year of age if unrecognized and untreated is not infrequent We have ... instance of treated staphylococcal ... effusion with sequellae of severe c... pericarditis leading to death under ... 1 year

The history is one of ... rapid ... febrile illness in an i... previ... been healthy Dysp... point to the heart and/or lungs The physical examination may reveal normal heart tones, no murmurs Hepatomegaly may be present but peripheral edema is not present

The electrocardiogram may be normal but often will show minimal changes of elevation of the ST segment and perhaps T wave changes The roentgenogram shows massive radio opacity which can be distinguished from cardiomegaly only by fluoroscopy at which procedure the complete absence of visible pulsations should create a strong suspicion of this diagnosis Pulmonary vasculature is normal The diagnosis of pericardial effusion may be confirmed by a pericardial tap If response to this simple procedure is not prompt and sustained, surgical drainage of the purulent material is indicated just as it is in most other purulent staphylococcus infections of the chest in the infancy age group

GLYCOGEN STORAGE DISEASE

Glycogen storage disease is a dominant hereditary trait The finding of this disease in other members of the family by history is diagnostic The history is similar to that described for myocarditis and endocardial fibrosis On physical examination these children invariably show severe wasting None are well developed as would often be the case in endocardial fibrosis or myocarditis When this disease involves the heart primarily, the life expectancy is rarely over 9 months of age This fact is important in eliminating suspicion of this disease in children over age 1

The electrocardiogram is said by some[14] to be different from that in endocardial fibrosis or myocarditis but in the one case that we have seen the changes were only those of myocarditis with changes in the ST segment and negative T ... the left precordium The roentgen... similar to those patients with ...rosis or myocarditis The diag... strongly suspected in a child wi... with no evidence ... a shunt and ... po... birth ... e the ... ves ... is, ... y of th... m ... ul ... ing ... pre... n

specific treatment for this disease The infant must be treated symptomatically The prognosis is poor for survival beyond a year of age when the heart appears to be primarily involved

ANOMALOUS CORONARY ARTERY ARISING FROM THE PULMONARY ARTERY

This anomaly has been rare in our large series of autopsied cases The clinical findings are similar to those mentioned above for endocardial fibrosis myocarditis and glycogen storage disease One exception is the appearance of attacks of paleness and what might be interpreted as precordial or abdominal pain by the reaction of the infant It is almost impossible to separate this malformation clinically from the others previously discussed Although the electrocardiogram is said to be suggestive of a myocardial infarction in the adult age range we have as yet seen no characteristic or pathognomonic electrocardiographic change The frequent combination of anomalous coronary artery from the pulmonary artery and endocardial fibrosis adds to the difficulty of diagnosis

Various procedures for establishing collateral circulation to the heart have been attempted in the treatment of these individuals To the best of my knowledge none of these have proved effective Edwards has proposed that the primary difficulty in this malformation may result from a left to right shunt from the coronary into the pulmonary artery and that the treatment would therefore be merely ligation of this vessel at its origin It has been suggested that the coronary artery could be transplanted to the aorta I know of no instance where this has been attempted as yet

CARDIAC TUMORS

Recently heart tumors have been reported more frequently in the literature[4] Rhabdomyomas of the heart muscle occur frequently in association with tuberous sclerosis The typical findings of tuberous sclerosis in the face of cardiac involvement should make one suspicious of a cardiac tumor Other tumors involving the heart muscle present a picture which in most instances has been indistinguishable from those malformations discussed in the previous paragraphs



Fig 12 Teratoma of the Heart in a Female Age 2 Months The massive enlargement of the cardiac silhouette was due in part to pericardial effusion Now 4 years old and well

Within the last few years we have seen one instance of a teratoma arising from the aorta intrapericardially The history was one of a 2 month old female who began having episodes of apnea and cyanosis lasting for short intervals with apparent normalcy in the interim

On physical examination the child appeared well developed and healthy and no heart murmurs were heard

The electrocardiogram was also within normal limits for the age The x ray showed massive cardiomegaly (Fig 12)

In this instance the finding of normal blood pressure the absence of left ventricular hypertrophy and strain pattern which are characteristic of endocardial fibrosis myocarditis glycogen storage or other heart tumors suggested to us the possibility that this child might have a heart tumor with pleural effusion She was sent for thoracotomy and an extremely large tense pericardium was noted on opening the chest When the pressure was relieved the heart action immediately improved Exploration revealed the presence of a tumor attached by a pedicle to the aorta and it was easily removed The heart size postoperatively was within normal limits This child recovered and has had no recurrence over the last 4 years



Fig 13 Double Aortic Arch in Male Age 5 Months This patient had dyspnea and recurrent pneumonias probably owing to partial obstruction of the trachea A B and C these films show the indentation of the aortic ring on the esophagus

In another instance an older child of 2 years was referred to our hospital because of vomiting, paleness, and rapid heart action

On physical examination this child was found to be extremely ill and the heart rate rapid

The electrocardiogram showed a marked arrhythmia which appeared to be supraventricular in nature Digitalization and other medical management was ineffective and this patient expired within 8 hours of his admission to the hospital

At autopsy a large tumor was found infiltrating the wall of the left ventricle

DOUBLE AORTIC ARCH AND VASCULAR ANOMALIES OF THE GREAT VESSELS

Such anomalies are seen frequently and are diagnosable by their characteristic indentation of the barium filled esophagus In our experience such vessels usually have not been accompanied by signs and symptoms of compression of the trachea or esophagus The most frequent anomalous vessel is the right subclavian artery arising from the descending arch of the aorta and crossing the esophagus obliquely and producing a characteristic roentgen picture Surgical treatment for this condition is rarely necessary

Difficulty in breathing a brassy croupy cough and sternal and intercostal retractions should suggest this diagnosis

Ordinarily there are no other physical signs and symptoms pointing to this lesion A heart murmur is absent or not significant

The diagnosis is established by a barium swallow during fluoroscopy (Fig 13) If it is important to the surgeons to know specifically the anatomical arrangement of these vessels a forward angiocardiogram will outline these structures nicely The retrograde aortogram has been uniformly disappointing Usually the experienced surgeons can accurately delineate the arrangement of the great vessels at the time of surgery and an angiocardiogram is not necessary In most instances the binding obstruction from the vascular ring may be removed by the surgeon The immediate results of surgery may not be as dramatic as one would expect We have seen an autopsy specimen in which the indentation made into the trachea by the vessel was still present so that there was no immediate relief of symptoms In this case it becomes important to tide the child through the postoperative period so that the trachea may grow with the growth of the child In the absence of a compressing mass the trachea will ultimately return to normal In our experience we have not seen associated intracardiac malformations associated with double aortic arch and presumably these infants that recover should therefore have a normal life expectancy



Fig 14 Congenital Mitral Stenosis with coarctation of aorta, Age 3 Years A The third curve of the left border of the heart is prominent, owing to enlargement of the left atrium B Lateral view shows marked left atrial and right ventricular enlargement

CONGENITAL MITRAL STENOSIS[52]

If the congenital mitral stenosis is severe, the left ventricle fails to develop an adequate cavity or hypertrophies to such an extent that the ventricular cavity is almost obliterated As a consequence, the aorta is small, and coronary arteries are supplied from retrograde flow from a patent ductus arteriosus These patients generally survive for a few days or at best a few months They are similar in all respects to the patients with aortic atresia or "non functioning left ventricle" described earlier

Less frequently a less severe form exists permitting longer survival Case report of one such patient follows A diagnosis of cyanotic congenital heart disease was made at birth Her condition gradually improved from birth so that she had no obvious cyanosis when she was first seen in our heart clinic at 7 months of age On physical examination a systolic murmur with no diastolic component was heard along the left sternal border

The electrocardiogram failed to show the expected right ventricular hypertrophy that one might see with mitral stenosis In fact, there was evidence of left ventricular hypertrophy on the original electrocardiogram Occasionally she developed episodes of supraventricular tachycardia and arrhythmias A change from a left hypertrophy pattern toward a right hypertrophy pattern gradually occurred

The x-rays showed large heart with an enlarged pulmonary artery segment and left atrium Pulmonary vascular markings were accentuated indicating a left to right shunt

Heart catheterization revealed the presence of a patent ductus arteriosus as demonstrated by a catheter passing through this defect into the descending aorta There was also a left to right shunt at the pulmonary artery level No differential oxygen values were obtained between the right brachial artery and femoral artery since a reversing patent ductus was not suspected The pressures in the pulmonary artery were of 100 mm of mercury systolic Since this child was under a year of age

Fig 15 Angiocardiogram of the above case of Congenital Mitral Stenosis shows A Contrast agent filling the right heart and pulmonary arteries and B Contrast agent filling huge left atrium



Fig 16 Congenital Mitral Stenosis Age 3 years Pulmonary artery pressure was 115/70 Mean wedge pressure 27 mm of Hg Roentgenogram shows left atrial appendage enlargement along left border of the heart

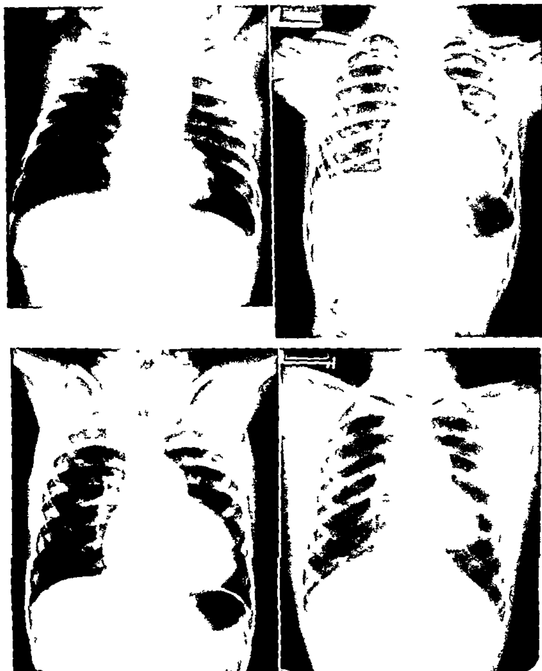


Fig 17 Isolated Pulmonary Stenosis with Intact Interventricular Septum A At the age of 5 months the picture is similar to tetralogy of Fallot B At 5 years of age the typical post stenotic dilatation of the pulmonary artery is present C At 9 years of age the right ventricular pressure was 260 0 This pre operative film shows an enlarged heart D At 16 years of age some seven years after his operation the heart size is within normal limits An enlargement of the left main pulmonary artery segment is still present The immediate post-operative right ventricular pressure was 66 0



Fig 18 Infundibular Pulmonary Stenosis in Female Age 8 Years A Angiocardiogram shows large undivided segment of the pulmonary artery associated with a massive enlargement of the right ventricle B Angiocardiogram shows infundibular stenosis of the right ventricle Intact interventricular septum proved by intracardiac surgery

it was felt that the presence of a patent ductus and severe hypertension without obvious reversal might be surgically correctable at this age but not if such an operation were defered

She had a thoracotomy The patent ductus arteriosus was ligated When the patient withstood this ligation for at least 30 minutes the patent ductus arteriosus was divided The patient made a fairly uneventful recovery from surgery but on the second to third postoperative week began to develop signs of right heart failure These were treated with a low salt diet and mercurial diuretics However the child never gained any weight and did not do well for several months She was recatheterized and it was found that the shunt had been closed but extreme pulmonary hypertension and increased pulmonary resistance were present

At autopsy it was found that she had a small opening for a mitral valve with underdevelopment of the left ventricle and a small aorta Marked intimal proliferation of the small pulmonary arteries and arterioles was found microscopically

We have also seen congenital mitral stenosis in association with several cases of ventricular septal defect When these have been recognized at surgery the mitral valve has been opened and the ventricular septal defect closed Their postoperative courses have been uneventful Post operative physiologic studies of these children have not been undertaken as yet In addition we have seen a case of severe mitral stenosis associated with coarctation of the aorta The diagnosis of coarctation of the aorta was made on the basis of blood pressure differential between arms and legs The diagnosis of mitral stenosis was strongly suspected because of the characteristic diastolic rumble at the apex Both of these defects were relieved at surgery and the patient did well postoperatively (Figs 14 15)

Isolated mitral stenosis is rare in our experience We have observed one such patient 3 years old The characteristic finding in this instance was a typical diastolic rumble of mitral stenosis The electrocardiogram showed marked right axis deviation and right ventricular hypertrophy The roentgenogram showed an enlarged heart with a mitral con

figuration and a large left atrium by barium swallow (Fig 16)

This patient had a systolic pressure of 115 mm of mercury in the pulmonary artery Although there was no left to right shunt present the patient had a femoral artery saturation of 84% Since there was no differential oxygen saturation between the brachial artery and femoral artery a reversing patent ductus did not seem likely

This patient was sent to surgery A small mitral valve was opened under direct vision The postoperative course was downhill and the patient expired No other intracardiac defects were found and the presence of cyanosis due to right to left shunt could not be satisfactorily accounted for at autopsy It seems entirely possible that if this diagnosis can be accurately determined at an earlier age these children may be salvaged by mitral valvulotomy

PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM AND INTACT ATRIAL SEPTUM

When cyanotic an infant with severe pulmonary valvular stenosis is easily recognized Such infants invariably have an associated patent foramen ovale Their pulmonary vascular flow is less than the systemic flow and is not included in this division of discussion

We have seen an instance of pulmonary valvular stenosis with both septa intact and having difficulty below a year of age[46]

This child when first seen at 5 months of age had been asymptomatic except for slight dyspnea The family physician had heard a loud systolic murmur

On physical examination the child was well developed and acyanotic The presence of a systolic thrill and murmur along the left sternal border was suggestive of a ventricular septal defect

The roentgenograms showed an enlarged heart The pulmonary vascular markings were at the upper limits of normal and consistent with the diagnosis of a ventricular septal defect Several months later she developed a series of convulsions and paleness The child appeared pale and extremely ill A murmur was again heard only along the left sternal border P_2 was not prominent at this examination The electrocardiogram was similar to the previous one and there was no marked right ventricular activity or left ventricular activity The P waves were prominent but not exceptional

The radiographs again showed the heart to be enlarged and the main pulmonary artery segment and the pulmonary vascular markings to be within normal limits in size

The correct diagnosis of pulmonary stenosis was suspected and confirmed by an angiocardiogram The child's state was critical An emergency thoracotomy was not successful and the child died At autopsy there was a small opening in the pulmonary valve of about 1 mm

The absence of even a normal right ventricular activity on the electrocardiogram and the absence of a poststenotic dilatation of the pulmonary artery by x ray made this diagnosis difficult Both of these findings are ordinarily associated with pulmonary valvular stenosis in older children and adults (Fig 17 A B C D) In such an instance a VR_4 lead or a positive T wave in lead V_1 may be helpful in determining the presence of right ventricular hypertrophy Perhaps the most helpful symptom is pale spells" and seizures with no apparent cause in a child with a systolic murmur Pale "spells" and seizures occurring in infancy represent a diagnostic and surgical emergency since the clinical course is usually rapidly downhill

Subacute bacterial endocarditis occurring under the age of five years in our experience has been almost invariably associated with pulmonary infundibular stenosis and intact septa[46] The history of low grade fever and listlessness is obtained On physical examination the children have been pale the liver and spleen were palpable A grade III rough systolic murmur and a normal pulmonary second sound have been prominent findings on the physical examination

The electrocardiogram has shown a right ventricular hypertrophy The roentgenograms show only a mild cardiac enlargement without exceptional pulmonary artery enlargement Pulmonary vascular markings have been within normal limits (Fig 18)

The diagnosis of subacute bacterial endo-

carditis was established by repeated blood cultures. Upon recovery from the subacute bacterial endocarditis, cardiac catheterization revealed a low pressure in the pulmonary artery with a very definite tracing of infundibular type stenosis and a high pressure of over one hundred in the right ventricle.

One such patient had intracardiac surgery by Drs. Lillehei and Varco. They were able to remove large sections of infundibular narrowing. The patient's postoperative recovery was uneventful. She was re-catheterized and the pressure had fallen in the right ventricle from the preoperative value of 110 to 44.

The second instance was almost identical in terms of history, physical examination, electrocardiogram and radiographic findings. He was referred to us 2 years after an attack of subacute bacterial endocarditis for physiologic studies. At the time it was impossible to enter the pulmonary artery, but the finding of high pressures in the right ventricle in conjunction with the radiographic findings made the diagnosis of pulmonary infundibular stenosis highly probable. At thoracotomy an unexpected finding was noted. The aorta arose from the left cardiac border in an anterior position, and the pulmonary artery arose posteriorly and to the right. This is a lesion known as "corrected transposition of the great vessels" with associated pulmonary stenosis. Because the coronary artery was anomalous and passed over right ventricle the usual right ventriculotomy could not be performed. The procedure was discontinued without definitive surgery. A subsequent angiocardiogram following his recovery confirmed the diagnosis of corrected transposition and is illustrated in the accompanying film (Fig. 19, A, B, C).[47]

EBSTEIN'S MALFORMATION OF THE TRICUSPID VALVE

This malformation consists of abnormal downward displacement of the tricuspid valve so that the effective right ventricle is a smaller cavity and the right atrium is a much larger cavity which includes ventricular musculature.

The characteristic textbook description of this malformation indicates that these children and adults are uniformly cyanotic. Their roentgenograms show diminished pulmonary vascular markings resulting from diminished pulmonary blood flow. With newer physiologic methods we have been able to make this diagnosis in young infants before cyanosis develops. At such times the pulmonary vascular markings are within normal limits as would be expected.

In more than a half a dozen of our cases seen in infancy, only one was cyanotic at the time of the diagnosis. She was an eight year old girl studied previously at 5 years of age and was acyanotic at that time. Only two of more than six cases studied had a history or finding of paroxysmal rapid heart action. This is apparently a phenomenon which occurs more frequently in the later age group. Most of our children have been asymptomatic early in life.[74]

On physical examination they appear normally developed and acyanotic. A diffuse soft heart murmur is heard over the precordium. It does not sound significant. The heart tones are often peculiar. A split first heart tone has been frequently heard.

The usual electrocardiogram shows complete right bundle branch block and peaked P waves. We have recently seen several patients with this malformation whose electrocardiogram showed the Wolff-Parkinson-White configuration, that is a short PR interval, delta wave and prolonged QRS complex. The ECG pattern is that of left axis deviation, left bundle branch block and negative T waves in the left precordial leads all suggesting left ventricular hypertrophy. The diagnosis of aortic stenosis may be suggested from these findings. The W-P-W findings on the ECG make the usual criteria for ventricular hypertrophy invalid. One infant died at 30 hours of age and the electrocardiogram already showed the typical complete right bundle branch block. This is apparently an early finding. As yet we have not discovered any anatomical variations correlating with this difference in pattern of the electrocardiogram. In one instance the presenting complaint at a few months of age was that of paroxysmal rapid heart action. The typical complete right bundle branch block pattern developed as this child was observed over the next 3 years. She developed clinical

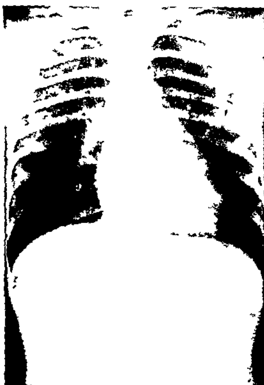




Fig 19 Corrected Transposition of the Great Vessels in a Male Age 9 Years A This posteroanterior view shows a radiograph similar to that seen in pulmonary stenosis B Angiocardiogram shows
s and
t and
from
the left atrium Often the mitral valve is deformed and an interventricular septal defect is present



Fig 20 Ebstein's Disease Posteroanterior *roentgenogram reveals generalized enlargement of* the heart and normal to decreased vascular shadows. The absence of left atrial enlargement distinguishes it from lesions of the left heart

nephrosis unresponsive to usual medical management and died within one month of the onset At necropsy the abnormally placed tricuspid valve typical of Ebstein's disease appeared to be stenotic

The roentgenograms have also been very helpful in the diagnosis of Ebstein's disease The heart shows a varying degree of enlargement and in most instances a square or boxy type heart with the left contour squared off (Fig 20) The pulmonary vascular markings are within normal limits or actually decreased The left atrium has not been enlarged unless there has been a marked right to left shunt at the atrial level with clinical cyanosis This same squared off contour of the heart also has been observed in the case of total anomalous pulmonary venous return In this entity the pulmonary vasculature is definitely increased ruling out Ebstein's malformation Pulmonary valvular stenosis with or without patent foramen ovale has frequently shown an enlarged squaring off of the left contour in the AP view and diminished pulmonary vascular markings On the basis of x rays alone these two defects may be impossible to separate In this instance the presence of complete right bundle branch block in the absence of a characteristic murmur of pulmonary stenosis would be helpful in establishing a strong suspicion of this diagnosis

Heart catheterization in Ebstein's disease is extremely valuable The finding of normal or only slightly elevated pulmonary artery pressure and normal right ventricular pressure rule out pulmonary valvular stenosis The change from normal to low ventricular pressure to right atrial pressure occurring when the catheter is definitely to the left of the spine is pathognomonic

At present no satisfactory surgery is available for this malformation The Blalock Taussig type of anastomosis has been attempted when the patients were cyanotic and had definite evidence of diminished pulmonary blood flow This operation has uniformly been inadequate Closure of the patent foramen ovale has been attempted and has resulted in clearing of the cyanosis and clearing of right heart failure [49] This closure forces all venous return through the tricuspid valve to the lung and make the right atrium a more effective pumper By means of direct vision intracardiac surgery a plication to eliminate the ventricular muscle which is present in the dilated right atrium has been proposed [49] At the present time this has as yet been untried

COR TRI ATRIATUM

This malformation consists of a stenosis of the pulmonary venous return as it enters the left atrium This malformation appears anatomically as if the left atrium were divided by a diaphragm into two parts This malformation is included in this classification only because there is no left to right shunt or right to left shunt and therefore pulmonary vascular flow is normal We have seen this malformation only in an older child but it has been reported in infants and children In our patient a soft grade II systolic murmur over the apex suggested an atrial septal defect

The electrocardiogram shows a right ventricular hypertrophy The roentgenograms are

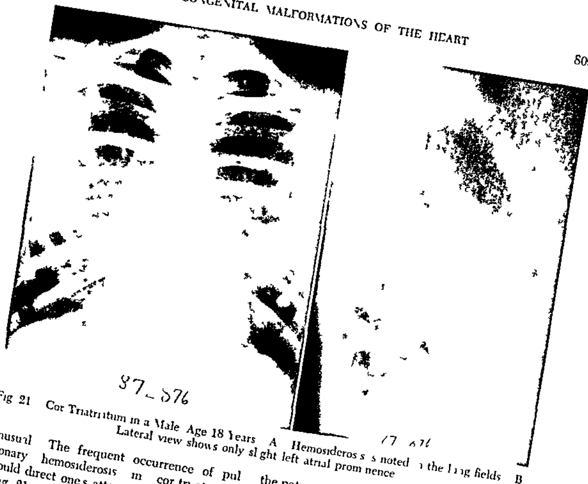


Fig 21 Cor Triatriatum in a Male Age 18 Years A Hemosiderosis is noted in the lung fields B Lateral view shows only slight left atrial prominence

unusual The frequent occurrence of pulmonary hemosiderosis in cor triatriatum should direct one's attention to this diagnosis (Fig 21 A B)

The physiologic studies on such a patient reveal the absence of a left to right shunt in the face of x ray findings which might suggest this when reviewed casually The pulmonary artery pressure in our patient was only mildly elevated at 40 mm of mercury but the patient had had episodes of pulmonary edema and hemoptysis which appeared to be out of proportion to this degree of pulmonary artery elevation if one were to consider this as a mitral valvular stenosis The finding of an exceptionally elevated pulmonary capillary or wedge pressure would be confirmative of this diagnosis in the presence of pulmonary vascular congestion

Intracardiac surgery makes it possible for the surgeon to remove the diaphragm separating the pulmonary veins from the mitral valve In our instance this was done successfully and the patient has had a very uneventful recovery and has had no further symptoms

PRIMARY PULMONARY HYPERTENSION

This is not a primary malformation of the heart but simulates it in many ways so that it must be discussed in connection with congenital heart disease In primary pulmonary hypertension a severe narrowing of small pulmonary arteries and arterioles by intimal proliferation occurs The pulmonary blood flow and systemic flow is ultimately reduced beyond that necessary to maintain life Secondary pulmonary hypertension resulting from a large ventricular septal defect single ventricle truncus arteriosus and other congenital malformations of the heart is recognized as a frequent or an almost invariable occurrence [0] In some instances pulmonary hypertension and an associated cardiac malformation occur in severe enough degree and at an early enough age so that the question of

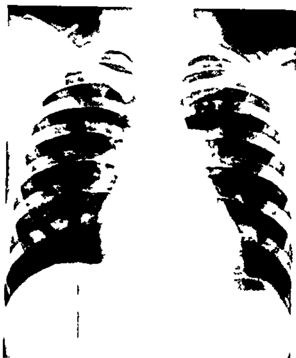


Fig 22 Primary Pulmonary Hypertension in a Female Age 12 Years Enlarged central pulmonary arteries without enlarged peripheral arteries are visualized

whether or not the pulmonary hypertension is secondary to the heart disease is a real unanswered question However it appears when pulmonary hypertension occurs with patent ductus arteriosus or with ventricular septal defect the defects have been large and as such are probably causative and not coincidental findings

The pulmonary hypertension in mitral stenosis or pulmonary venous stenosis may also account for some cases and should not be classified as primary pulmonary hypertension

There have been some 2 to 5 year old patients with pulmonary hypertension without associated anomalies dying from right heart failure Ordinarily this disease manifests itself in the older age patient

The history obtained is that these children frequently have grown well but then their growth has slowed down Easy fatiguability and dyspnea on exertion are frequent symptoms Precordial pain has been a frequent finding in both older children and adults but has not been as noticeable in the younger age group

On physical examination there is often a right precordial bulge The pulmonary second sound is markedly accentuated There may be no significant heart murmurs However many times there are diffuse systolic murmurs heard over the precordium particularly at the apex characteristic and suggestive of a rheumatic myocarditis

The electrocardiogram especially toward the end stages shows a peaked P wave and marked right ventricular hypertrophy

The roentgenogram and fluoroscopy reveal an enlarged heart with normal pulmonary vascular markings In some instances the hilar shadows are large and even at first examination suggest the presence of increased pulmonary flow Both in the adult or older child large hilar vessels and sparse peripheral vessels are suggestive of pulmonary hypertension However the younger the infant the less valid is this sign The undivided segment of the pulmonary artery is ectatic The diagnosis of pulmonary valvular stenosis with poststenotic dilatation has been most often confused from a roentgen point of view The clinical finding of an exaggerated pulmonary second sound is helpful in ruling out the diagnosis of pulmonary valvular stenosis (Fig 22)

The physiologic studies of heart catheterization are the most helpful in establishing the presence of pulmonary hypertension In the right ventricle and pulmonary artery elevated pressure usually greater than the systemic pressure is found If right ventricular pressure is equal to the systemic pressure the situation of balanced pressures may exist resulting from a ventricular septal defect or a patent ductus arteriosus Here there is no constant left to right or right to left shunt However usually children with ventricular septal defect even in the face of a balanced pulmonary artery aortic pressure show a noticeable left to right shunt This shunt is not found as consistently in patent ductus arteriosus However the patent ductus can be detected by passing the catheter through the ductus or by taking simultaneous oxygen samples from both the right brachial and femoral arteries Severe atypical mitral stenosis may give all the physiological findings of primary pulmonary hypertension It is therefore important to obtain a





Fig 23 Pulmonary Arteriovenous Fistula in a Male Age 13 Months A Density in the right lower middlung field represents arteriovenous fistula B Angiogram shows pulmonary arterial phase C Pulmonary venous phase is shown

normal pulmonary capillary ("wedge") pressure to exclude this diagnosis

For primary pulmonary hypertension there is no effective medical or surgical treatment other than supportive therapy

PULMONARY ARTERIOVENOUS FISTULA

In this condition desaturated pulmonary artery blood bypasses capillaries to enter pulmonary veins and systemic circuit without



Fig 24 Congenital Methemoglobinemia and Normal Heart and Lungs in a Female, Age 12 Days This patient was cyanotic since birth She had never left the nursery No history of aniline dye markers on diapers or other toxic agents Methemoglobinemia cleared on administration of methylene blue and recurred after withdrawal of methylene blue A Normal posteroanterior view of heart and lungs Normal angiocardiogram is illustrated on this patient in Figure 1

oxygenation The patient is therefore cyanotic when pulmonary flow is equal to systemic flow

The 13 month old male patient whose roentgen film is illustrated (Fig 23A, B, C) had poor weight gain since birth He was slightly dusky A very soft continuous murmur was heard posteriorly only when the child was asleep The ECG showed left ventricular hypertrophy

Because of the poor weight gain this child was advised to have a thorocotomy to remove *this segment of the lung* Unfortunately the child did not tolerate the procedure well and expired shortly following the procedure Our experience with this malformation has been small with no resultant cures Removal of *small* roentgenographically visible areas has resulted in temporary relief After a period other angiomatous areas become prominent

METHEMOGLOBINEMIA

Cyanosis in the first two weeks of life may result from methemoglobinemia due to nitrite intoxication from use of well water or rarely from a congenital presence of this substance presumably due to an inborn absence of an essential enzyme necessary for hemoglobin metabolism

"Well water" methemoglobinemia may have its onset 3 to 4 days following discharge of the infant from the newborn nursery The history will be that the baby gradually is noted to become cyanotic with few other symptoms early in the condition The formula is prepared *from well water which has been thoroughly* boiled to reduce bacterial contamination but thereby concentrates the nitrite content

On physical examination the cyanosis is evident with marked mottling of the skin A heart murmur is absent The electrocardiogram is normal The roentgenogram is normal In the presence of cyanosis in the history the normal roentgenogram is often felt to be compatible with tetralogy of Fallot, particularly if the radiologist is unaware of the normal sparsity of pulmonary vasculature in the normal infant (Fig 24)

The diagnosis of methemoglobinemia may be established simply by pricking the finger of such an infant and placing the blood on a piece of white filter paper next to a known normal for control With oxygenation the normal blood becomes bright red, the blood containing methemoglobin remaining a chocolate brownish color Quantitative values may be obtained by spectroscopy

In most instances treatment consists merely of discontinuation of the source of the nitrite intoxication usually the well water If symptoms of dyspnea and cyanosis are more prominent the use of intravenous methylene blue will produce a dramatic and lasting return to normal of the capacity of the hemoglobin to oxygenate fully

Congenital methemoglobinemia has been encountered only once in our clinic Cyanosis was noted prior to discharge from the hospital nursery No history of drug intake in either the mother or the baby was elicited No contact with toxic agents known to produce methemoglobinemia could be obtained

On admission the cyanosis was marked No murmur was heard The blood pressure was normal Peripheral pulses were normal The electrocardiogram showed right hypertrophy consistent with her age The roentgenograms were within normal limits and felt to be compatible with tetralogy of Fallot in the presence of clinical cyanosis An angiocardiogram showed normal right and left sided anatomy

The diagnosis was confirmed by determination of methemoglobin levels in the blood Oral methylene blue has maintained this child free of cyanosis with normal growth and development for the past 2 years

CONGENITAL HEART BLOCK[30]

Some children are born with a slow heart rate but in all other respects may be normal About one half the instances of slow heart rate due to congenital heart block have associated congenital malformations of the heart This may occur with any malformation but quite frequently with "corrected transposition of the great vessels" The outlook for these patients is determined by the severity of the associated anomaly



Fig 25 Congenital Heart Block (Pulse 52 min) A slightly enlarged heart is also seen with bradycardia The reason for the prominent pulmonary arteries and generalized enlargement of the heart could not be detected by heart catheterization A systolic murmur (grade 3) was present

About one half the patients seen with congenital heart block are asymptomatic There is often a systolic murmur along the left sternal border suggestive of a ventricular septal defect The electrocardiogram shows complete atrioventricular dissociation with independent auricular and ventricular rates The ventricular rates are constant for each individual and do not vary noticeably with exercise The constant rate is usually about 50 per minute

The roentgenogram (Fig 25) may show a slight to moderate overall enlargement The pulmonary artery segment is usually prominent and pulmonary vasculature prominent The left atrium may be prominent The overall roentgen picture simulates ventricular septal defect When the radiologist notices the slow heart rate at fluoroscopy he should be more aware of the cause of the abnormal findings seen on the film study Cardiac catheterization of this group of patients has revealed no shunts and pressures which are normal or only slightly



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Fig. 27 Tetralogy of Fallot in Female Age 2 Years A Radiograph shows a right aortic arch and diminished pulmonary vasculature B Angiocardiogram shows aorta and narrowed right outflow tract filling from right ventricle Note trabeculated right ventricle C Aorta fills also from smooth walled left ventricle

the precordial leads but may show a positive T wave which under one year of age suggests right ventricular hypertrophy[34] The roentgenogram often shows a normal cardiac silhouette However the concave pulmonary artery segment elevated apex and diminished vascularity of the lung fields so typical in the older patient may be present (Figs 27A B C and 28A B)

The characteristically small heart is felt to be due to the rarity of right heart failure because the ventricular septal defect permits emptying of the right ventricle Occasionally tetralogy of Fallot is seen with larger heart



Fig 26 Diverticulum of left ventricle Male age 11 years Normal contour of the heart on the roentgenogram Pulsating mass seen above the umbilicus on the physical examination

elevated in the pulmonary artery and right ventricle This has been attributed to the large stroke volume which in effect produces an increased flow rate during the ejection phase of the cycle

The prognosis for the pediatric age range has been good The overall life expectancy has also been quite favorable although a few such patients have been reported to have Adams Stokes attacks and sudden unexpected death

DIVERTICULUM OF THE LEFT VENTRICLE

A very unusual anomaly of the heart which should be discussed because it is so readily diagnosed clinically and is surgically curable is a diverticulum of the left ventricle We have seen one such boy eleven years old who had been asymptomatic all his life At birth a pulsating mass was observed below the xiphoid process and above the umbilicus (Fig 26) Except for this mass the physical examination was negative The electrocardiogram was normal The few other cases reported had a left bundle branch block which cleared when the diverticulum was resected[61] The roentgenogram appeared to be within normal limits except for a mass below the diaphragm not specifically diagnostic Because of the similarity to reported cases in the literature he was sent for thorocotomy at which time the diverticulum which arose from the left ventricle was uneventfully excised

The prognosis without surgery is usually very limited because of spontaneous rupture in the first years of life

CONGENITAL MALFORMATIONS OF THE HEART WITH DIMINISHED PULMONARY BLOOD FLOW

For all practical purposes, patients who have diminished pulmonary blood flow by x ray and physiologically have varying degrees of clinical cyanosis or desaturation Of these groups the Tetralogy of Fallot is the commonest and best known combination of malformations

TETRALOGY OF FALLOT

In the older age group the clinical the electrocardiographic the radiographic and physiologic findings are well known and will not be repeated here[53] A considerable number of infants with this malformation in a severe form require immediate treatment otherwise they will not survive to an optimum age for surgical intervention In the infant the history and physical findings are similar to those found in the adult with the following differences The onset of progressive cyanosis of dypsneic spells and of failure to gain weight begins earlier On physical examination a severe degree of pulmonary stenosis may produce a much softer murmur than typical for the classical tetralogy of Fallot The electrocardiogram may not show a high R wave in VI of





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Fig 28 Severe Tetralogy of Fallot in Female Age 4 Months A Typically main pulmonary artery segment and branches are small B Angiocardiogram shows infundibular stenosis with aorta filling from right ventricle

size and various degrees of heart failure In this circumstance cardiomegaly and heart failure are due to the small size of the ventricular septal defect compared to the aortic orifice and is inadequate in size to permit complete emptying of the right ventricle

When the patient's condition is rapidly deteriorating we prefer an angiocardiographic study rather than heart catheterization in the small infant This study shows the anatomy of the outflow tract of the right ventricle and confirms the diagnosis For establishing this diagnosis angiocardiographically the 10 degree right anterior oblique (LPO) view is the best The actual *infundibular narrowing is* often visualized When uncertain whether you are dealing with a tetralogy of Fallot or pulmonary valvular stenosis with patent foramen ovale or transposition of the great vessels with pulmonary stenosis the right posterior oblique (LAO) position outlines the great vessels to better advantage

Under a year of age treatment for tetralogy of Fallot by the extra cardiac Blalock or Potts type of anastomosis has been less satisfactory than this same operation in the older age group [55] At the present time at the University of Minnesota patients in several age groups are being followed in whom intracardiac closure of the ventricular septal defect and resection of the infundibular area of the right ventricular outflow tract has been accomplished Preliminary studies indicate that this type of operation is successful and practical in the infant *It is interesting to note in this regard* that all patients with this malformation that have been operated upon by the surgical department of the University of Minnesota have *had their ventricular septal defect in the* usual place in the membranous septum and its clo

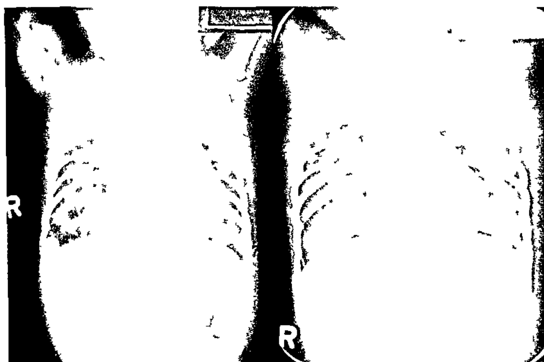


Fig 29 Tetralogy of Fallot A At 5 months of age the roentgenogram showed increased pulmonary vascularity He was acyanotic and asymptomatic with a loud heart murmur B At 18 months he was dyspneic cyanotic and squatted His roentgenogram showed decreased vascularity consistent with tetralogy of Fallot

sure in the usual manner leaves the aorta arising from the left ventricle as in any other heart It is therefore our feeling at the present time that the designation of dextro rotation of the aorta is of little surgical significance in the majority of cases We feel that the inclusion of this defect in the definition of tetralogy adds nothing and continues to remain a source of confusion which at the time of this writing serves no useful purpose and is of no surgical significance when a curative procedure is undertaken

Taussig has recently pointed out that certain children early in life exhibit cardiomegaly and evidence of increased pulmonary blood flow When these children are followed for one to two years the heart becomes smaller and assumes a typical roentgen picture of tetralogy of Fallot with diminished pulmonary vascularity (Fig 29) Gasul [9] reports three cases with physiological data which supports the concept of progressive stenosis in association with an interventricular septal defect Clinically and physiologically these unusual cases appear early in infancy to have minimal or no pulmonary stenosis and present as uncomplicated ventricular septal defects We have catheterized several infants with ventricular septal defects who exhibited a minimal degree of pulmonary stenosis Subsequently they were successfully operated so that we are unable to determine whether they might have fallen in the typical tetralogy of Fallot group or whether they might have become stabilized and present as an "acyanotic tetralogy of Fallot This entity will be discussed later under the heading of "Malformations with Increased Pulmonary Blood Flow "

PULMONARY VALVULAR STENOSIS WITH PATENT FORAMEN OVALE

In a less severe form this malformation of the heart is frequently found in older children and adults However as in many of the other malformations the finding of a severe degree



Fig 30 Valvular Pulmonary Stenosis with Patent Foramen Ovale in Female Age 3 Years Patient was severely cyanotic Right *ventricular systolic pressure was 105 mm of Hg A Before surgery* there was a generalized enlargement of the cardiac silhouette B Two years after surgery a large pulmonary artery is still visualized

of pulmonary valvular stenosis manifests itself in the young infant This is a potentially curable type of malformation which is difficult to recognize [9]

These children often give a history of cyanosis beginning from the first few days of life *In many instances they are severely cyanotic infants* A history of rapid breathing may be obtained

On physical examination there may be no heart murmur or only a soft murmur not localized to the pulmonic area

The electrocardiogram may show a right axis a normal axis or a *left axis* The P waves are ordinarily peaked The R wave in V_1 of the precordial leads may not be increased in amplitude However the presence of a positive T wave in V_1 *may be helpful In the* absence of right ventricular hypertrophy it may be impossible to separate severe pulmonary stenosis from pulmonary atresia and *tricuspid atresia The roent*genograms and cardiac fluoroscopy may reveal a cardiomegaly However until a year of age or later, the pulmonary artery segment is not prominent because of the absence of the typical poststenotic dilatation The pulmonary vascular markings are ordinarily diminished but if the child is in heart failure some degree of congestion may *not make this fact as evident as one might* expect (Fig 30)

The diagnosis can be confirmed by an angiocardiogram in the right posterior oblique position Here one sees the bolus of opaque media entering sequentially the right atrium the left atrium the left ventricle and the aorta arising *in a normal position If one can see* the pulmonary artery or the narrowed outflow tract of the right ventricle opacified at the same time it is helpful in establishing this diagnosis *In many instances however* the aorta and the pulmonary arteries opacify at the same time so one cannot be sure that they are *not being supplied through a patent* ductus arteriosus in the presence of pulmonary valvular atresia At cardiac catheterization a small

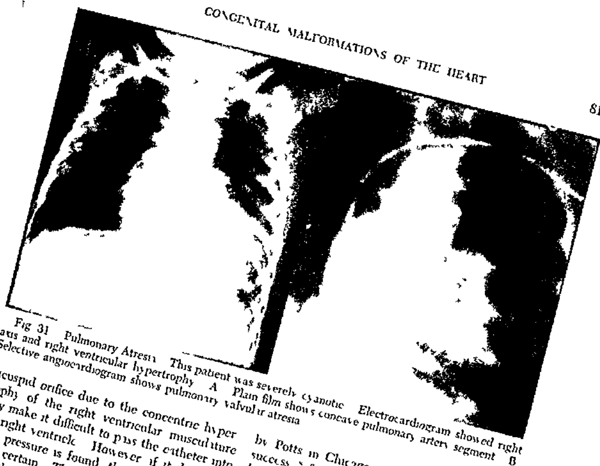


Fig 31 Pulmonary Atresia This patient was severely cyanotic Electrocardiogram showed right axis and right ventricular hypertrophy A Plain film shows concave pulmonary artery segment B Selective angiocardiogram shows pulmonary valvular atresia

tricuspid orifice due to the concentric hypertrophy of the right ventricular musculature may make it difficult to pass the catheter into the right ventricle However if it does and high pressure is found then the diagnosis is more certain The injection of opaque media with the catheter in the right ventricle should demonstrate the fine jet of the pulmonary valvular obstruction

When a child is referred with this malformation at an early age because of heart failure "pale" spells blue spells or seizures the course frequently is rapidly downhill The presence of severe pulmonary stenosis in a young infant with clinical symptoms is an indication for urgent surgical intervention The Blalock Taussig type of extracardiac anastomosis has been clearly shown to be ineffective in patients with pulmonary stenosis and an intact ventricular septum A valvulotomy by the Brock procedure is satisfactory in those children having a large right ventricle and nearing a year of age In the hands of our surgeons the Brock valvulotomy procedure has had to very discouraging results in the smaller patient with a very severe pulmonary stenosis A modified type of Brock procedure has been employed by Potts in Chicago in this age group with success [illegible] Because many of these patients have very thick right ventricular musculature there appears to be an associated infundibular outflow obstruction secondary to this muscular hypertrophy Because of this obstruction our surgeons have recently been attempting intracardiac correction but additional experience will be needed before this surgical procedure can be finally evaluated

A lesion similar to the malformation of extreme pulmonary valvular stenosis with patent foramen ovale is pulmonary valvular atresia with non functioning right ventricle This has been classified into two types [illegible] Type A is that in which the right ventricular muscle has hypertrophied to such an extent that the cavity is almost obliterated Type B has a fairly normal sized right ventricular cavity secondary to some degree of tricuspid valvular insufficiency or perhaps to a pin point opening in the diaphragm covering the pulmonary valve which has not always been recognized by the pathologist We have found it extremely difficult to separate the three above mentioned entities in all instances by methods presently available to us If the catheter en

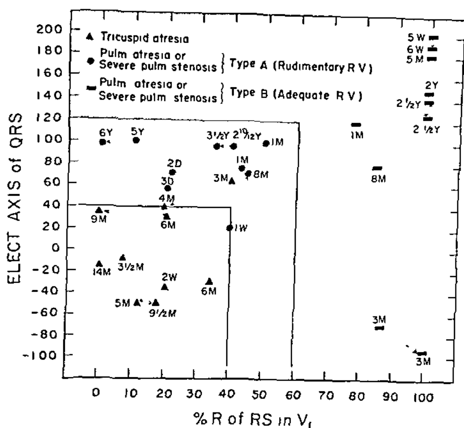


Fig 32 Graph of ECG

be placed into the right ventricle, tricuspid atresia is thereby eliminated If one is successful in injecting opaque media into the pulmonary arteries, this rules out pulmonary atresia However, often the right ventricle is not entered and selective angiocardiography or pressures are of little value in differentiating these three entities (Fig 31) If there is definite left axis deviation and no evidence of right ventricular activity on the electrocardiogram, the working diagnosis should be tricuspid atresia

Autopsy proved cases of pulmonary atresia with intact ventricular septum (Type A and Type B) and severe pulmonary stenosis with intact ventricular septum have revealed consistent differences which separate these anatomical variations[f] The axis deviation is plotted on the vertical axis and the percentage R to total RS wave in V_1 on the horizontal axis (Fig 32) Tricuspid atresia shows an axis deviation of less than plus 40° and per cent R/RS in V_1 of less than 40% Pulmonary atresia with a very small inadequate right ventricle (Type A) had an axis deviation of more than plus 40° and less than plus 120° and a per cent R/RS in V_1 of more than 40% and less than 60% Pulmonary atresia with a larger more adequate right ventricle or severe pulmonary stenosis with an adequate right ventricle had either marked right axis deviation or marked right ventricular hypertrophy as evidenced by a high per cent R/RS in V_1 The larger the right ventricular cavity the more right ventricular activity as expressed by a higher percentage of R/RS in V_1 At the present time pulmonary valvular atresia type A and tricuspid atresia cannot be cured by intracardiac surgery

EXTREME TETRALOGY OF FALLOT WITH PULMONARY VALVULAR ATRESIA "PSEUDOTRUNCUS"

In this type of malformation all clinical findings are similar to those seen in infants with



Fig 33 Pseudotruncus in Male Age 2 Months Angiocardiogram shows large interventricular septal defect pseudotruncus and patent ductus arteriosus



Fig 34 Truncus Arteriosus Type 4 in Female Age 4 Weeks This patient was cyanotic A No pulmonary artery segment is visualized B Angiocardiogram [illegible] no central pulmonary artery [illegible]

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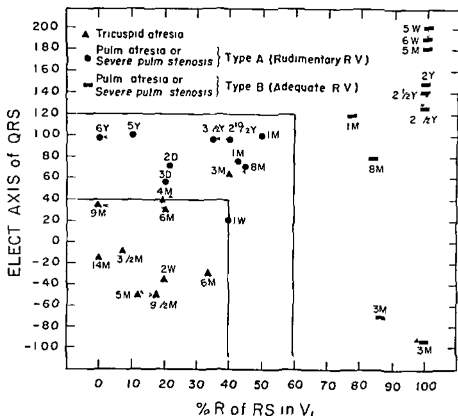


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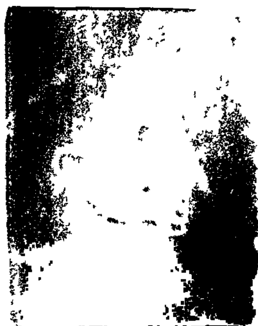


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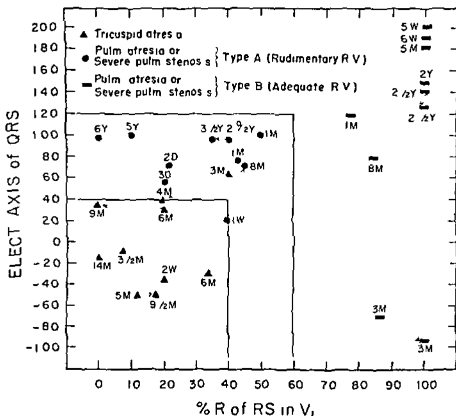


Fig 32 Graph of ECG

be placed into the right ventricle tricuspid atresia is thereby eliminated If one is successful in injecting opaque media into the pulmonary arteries this rules out pulmonary atresia However often the right ventricle is not entered and selective angiocardiography or pressures are of little value in differentiating these three entities (Fig 31) If there is definite left axis deviation and no evidence of right ventricular activity on the electrocardiogram the working diagnosis should be tricuspid atresia

Autopsy proved cases of pulmonary atresia with intact ventricular septum (Type A and Type B) and severe pulmonary stenosis with intact ventricular septum have revealed consistent differences which separate these anatomical variations[6] The axis deviation is plotted on the vertical axis and the percentage R to total RS wave in V_1 on the horizontal axis (Fig 32) Tricuspid atresia shows an axis deviation of less than plus 40° and per cent R/RS in V_1 of less than 40% Pulmonary atresia with a very small inadequate right ventricle (Type A) had an axis deviation of more than plus 40° and less than plus 120° and a per cent R/RS in V_1 of more than 40% and less than 60% Pulmonary atresia with a larger more adequate right ventricle or severe pulmonary stenosis with an adequate right ventricle had either marked right axis deviation or marked right ventricular hypertrophy as evidenced by a high per cent R/RS in V_1 The larger the right ventricular cavity the more right ventricular activity as expressed by a higher percentage of R/RS in V_1 At the present time pulmonary valvular atresia type A and tricuspid atresia cannot be cured by intracardiac surgery

EXTREME TETRALOGY OF FALLOT WITH PULMONARY VALVULAR ATRESIA "PSEUDOTRUNCUS"

In this type of malformation all clinical findings are similar to those seen in infants with



Fig 33 Pseudotruncus in Male Age 2 Months Angiocard ogram shows large interventricular septal defect pseudotruncus and patent ductus arteriosus





Fig 34 Truncus Arteriosus Type 4 in Female Age 4 Weeks This pat e it was cyanot c A No pulmonary artery segment is visualized B Ang oc ird ogram reveals no central pulmonary artery

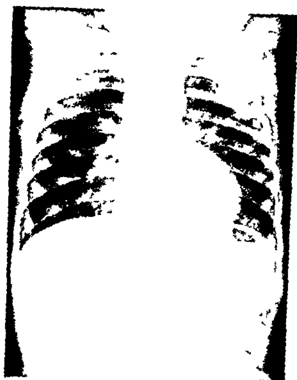






Fig 35 Tricuspid Atresia in Female Age 5 Years A The small pulmonary artery segment and enlarged left side of the heart simulates the radiographic findings in tetralogy of Fallot B and C Angiocardiogram shows contrast agent successively filling right atrium left atrium, left ventricle and aorta

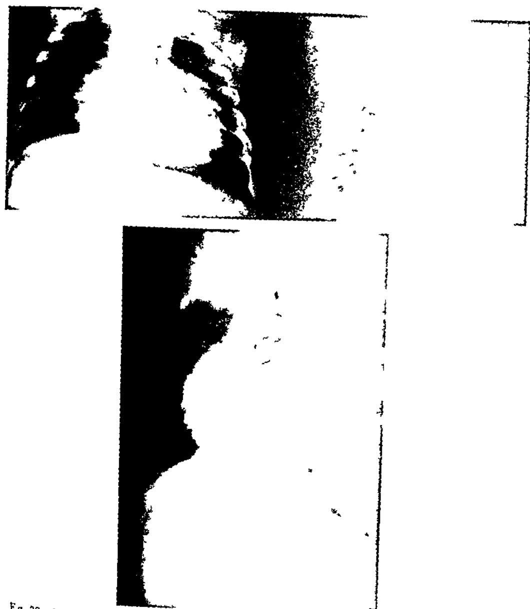


Fig 36 Tricuspid Atresia in Female Age 5 Months The patient showed deep cy... ...ctrocardiogram showed peaked P waves and left axis deviation and hypertrophy A Calcification ... the left ventricle and a generalized enlargement of the cardiac silhouette are seen B Right lateral view C Angiocardiogram shows dye in the right atrium left atrium left ventricle and great vessels

severe tetralogy of Fallot In the older age child one can often hear the continuous murmur of bronchial collateral and see the extremely large aorta or trunk at fluoroscopy However in the young infant, those two signs are not ordinarily present If an angiocardiogram is obtained in the left posterior oblique position, the obstructed outflow tract does not communicate with the main pulmonary artery segment and this segment fills from the aorta (Fig 33)

Some patients with this defect have a right and left main pulmonary artery and an undivided segment of the pulmonary artery When this is the case the surgeons are able to anastomose the pulmonary artery to the right



Fig 37 Tricuspid Atresia Interventricular Septal Defect Ostium Primum and no Pulmonary Outflow Tract Obstruction Female Age 6 Weeks Clinically acyanotic but *desaturated* *A Antero* posterior roentgenogram shows enlarged heart and slight increase in pulmonary vasculature simulating transportation of the great vessels

Fig 38 Congenital Absence of the Inferior Vena Cava in Male Age 1 Month Contrast agent is seen flowing to the heart via the azygos system

ventricle so that the pulmonary blood flow is increased even though there is no effective valve *In some instances a graft may be necessary* between the right ventricle and the right and left main pulmonary arteries The effect of the absence of a pulmonary valve cannot be finally evaluated at this time In dogs experimental work indicates that complete pulmonary valvectomy does not alter their well being

TRUE TRUNCUS TYPE IV (EDWARDS)[31]

True truncus type IV as defined by Edwards differs very little physiologically from the extreme tetralogy of Fallot with pulmonary valvular atresia or "pseudotruncus The main anatomical difference is the absence of both the undivided pulmonary artery segment and its main branches Because of the absence of the pulmonary arteries the surgeon cannot connect the pulmonary arteries to the right ventricle *Often with pleurectomy and thoro*cotomy alone these children improve because of the increased vascularization of the lung formed from collaterals Because of the similarity of all findings this malformation has been difficult to separate from the extreme tetralogy of Fallot (Fig 34) Since it is an infrequent anomaly such a patient deserves exploration for the presence of a small pulmonary artery

TRICUSPID ATRESIA

The essential clinical electrocardiographic roentgen and angiocardiographic findings present in this malformation have been discussed above under pulmonary valvular atresia type A (Figs 35A B C and 36A B C) In a child who is cyanotic and has a small heart the find

ing of a left axis deviation the absence of right ventricular activity and presence of left ventricular hypertrophy will be usually diagnostic of tricuspid atresia Wittenborg[64] has pointed out that many cases of tricuspid atresia will present with malrotation of the heart and dextrocardia At present the Blalock Taussig extracardiac anastamosis is the only procedure that has been found helpful and this less successful than for a regular tetralogy of Fallot

Usually tricuspid atresia will show diminished pulmonary vascular markings on the roentgen examination This finding may be less prominent if there is a ventricular septal defect and only a mild associated subpulmonary stenosis as is frequently the case If there is a ventricular septal defect and no pulmonary stenosis increased pulmonary vascular markings are present radiographically (Fig 37) Such a patient may simulate in all clinical respects the syndrome of tricuspid atresia associated with transposition of the great vessels[73] This latter group of cases will be discussed briefly under Malformations of the Heart Showing Increased Pulmonary Blood Flow However in simple tricuspid atresia one would see the aorta filling from the left ventricle and the pulmonary arteries filling in their usual position if angiocardiographic studies were adequately performed

SINGLE VENTRICLE WITH RUDIMENTARY CHAMBER FROM WHICH THE PULMONARY ARTERY ARISES

This malformation is physiologically almost identical to that of tricuspid atresia with ventricular septal defect However as frequently seen in single ventricle this malformation may differ in that the great vessels are frequently transposed or malrotated in such a way that the aorta lies anterior We have seen children with single ventricle and pulmonary stenosis who have reached the teen ages with relatively little difficulty In these children the degree of pulmonary stenosis protects the lungs from the arteriolar-sclerosing effects of the common ejectile force of the single ventricle This probably accounts for their apparent better prognosis The evidence of pulmonary stenosis is often mild enough so that on the roentgenogram there is actual evidence of some increase in pulmonary vascular markings and increased pulmonary flow These children show roentgen findings similar to tetralogy of Fallot in that the undivided segment of the pulmonary artery is not prominent However they generally have larger sized hearts and the pulmonary vascular markings are normal or slightly increased It is often difficult to establish this diagnosis with certainty either with forward angiography or heart catheterization unless both great vessels are entered

At the present time no surgically curable type of procedure has been devised for such patients The protection that the lungs have had from the outflow obstruction would seem to make these patients better candidates for the insertion of a ventricular septum when the surgeons have arrived at this point technically

TRANSPOSITION OF THE GREAT VESSELS WITH PULMONARY STENOSIS

We have seen only a few cases of this combination of defects From all outward appearances these patients have simulated the tetralogy of Fallot On the angiocardiogram the aorta fills directly from the right ventricle The aorta is in an anterior position The findings are not always distinctive enough in the left anterior oblique position to separate it with certainty from an extreme tetralogy of Fallot with pulmonary atresia or "pseudotruncus This malformation is inoperable at the present time

LEVOCARDIA WITH ABDOMINAL SITUS INVERSUS[5]

Levocardia with abdominal situs inversus has been usually associated with intracardiac malformations which include pulmonary stenosis Accompanying the pulmonary stenosis there has frequently been a large atrial and ventricular septal defect amounting to a cor biloculare or large atrioventricular communis In addition other anomalies of pulmonary venous return and coronary arteries have been reported These patients may be

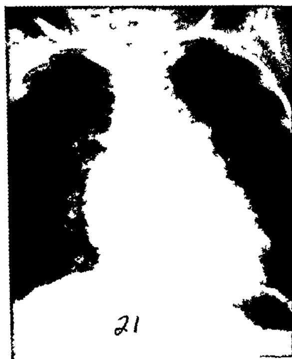


Fig 39 Patent Ductus Arteriosus in Male Age 3 Years A large pulmonary artery increased pulmonary vasculature and a large aorta are visualized characteristic of patent ductus arteriosus

referred for consultation when the heart appears normal in size and the pulmonary vascular markings diminished so that findings would be consistent with tetralogy of Fallot However the finding of a situs inversus of the abdominal viscera should make one extremely suspicious of other complicated lesions Because of this it is unlikely that such a defect would be susceptible to intracardiac curative procedures with the present state of our knowledge

A similar group of complicated congenital malformations of the heart have been associated with the finding of an absent spleen[33] The heart may be in the midline because of malrotation without obvious dextro or levo cardia A transposition of the stomach only may be found If one encounters this unusual occurrence without complete situs inversus of abdominal viscera this group of defects should be considered Peripheral blood smears show findings such as Howell Jolly" bodies typical of those found in postsplenectomized patients[34] If the hematologist can suggest that the peripheral smear is suggestive of an absent spleen then such a diagnosis may be suspected and findings at angiocardiography or heart catheterization may be more readily understandable

ABSENCE OF THE INFERIOR VENA CAVA

This anomaly has been encountered in six instances in our clinic[33] Variable intracardiac malformations have been present with pulmonary stenosis a frequent finding The clinical findings suggest usually tetralogy of Fallot We have as yet discovered no clue to make us suspicious of the correct diagnosis prior to angiography When the contrast agent is injected into the malleolar or saphenous vein the flow of the opaque agent into the vertebral and azygos system and emptying into the heart from above through the superior vena cava is characteristic (Fig 38) At present the presence of complicated intracardiac malformations ordinarily contraindicate intracardiac curative procedures

MALFORMATIONS OF THE HEART SHOWING INCREASED PULMONARY BLOOD FLOW

This group of malformations may be divided roughly into those having predominantly a left to right shunt clinically acyanotic and those who have both a right to left as well as left to right shunt clinically desaturated or cyanotic If the pulmonary blood flow is increased in patients with bidirectional shunts there is relatively more fully oxygenated blood mixing with desaturated venous blood This may produce systemic desaturation not always clinically noticeable as cyanosis

PATENT DUCTUS ARTERIOSUS[3]

Like many of the malformations already discussed in this chapter, most patients with pat

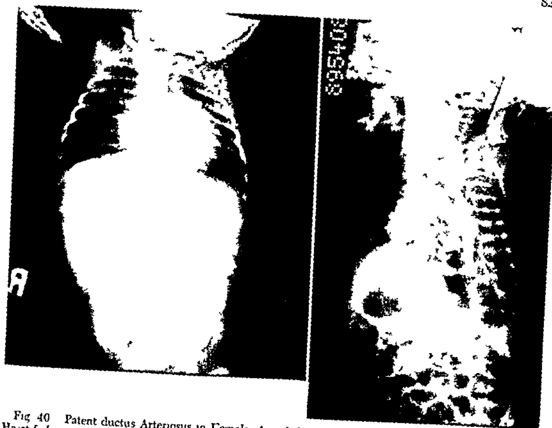


Fig 40 Patent ductus Arteriosus in Female Age 1 Month The patient failed to gain weight Heart failure occurred A Roentgenogram shows a nonspecific cardiac enlargement B Retrograde aortogram shows filling of the pulmonary vasculature via the aorta The ductus was ligated and the patient did well

ent ductus arteriosus are relatively asymptomatic throughout the early portion of their life However approximately 5 to 10% of the patients having a patent ductus arteriosus do present with severe clinical symptoms and signs and may succumb to their defect at an early age In premature children a large patent ductus arteriosus occurs more frequently than other types of malformations If an infant succumbs under three months of age the pathologists have generally considered the finding of a patent ductus to be a physiologic finding when there has been an adequate explanation for death from other causes However there is a group of patients in whom a large patent ductus arteriosus is found and whose primary signs and symptoms prior to death have been heart failure pneumonia and cardiomegaly Patent ductus has many features similar to those of infants in difficulty with a ventricular septal defect or an atrial ventricular canal These similar findings include failure to gain weight frequent pneumonias not responding well to medical management and a systolic heart murmur On the roentgenogram cardiomegaly with a prominent pulmonary artery segment left atrial enlargement and engorgement of the pulmonary vascular markings are seen (Figs 39 and 40A B) In fluoroscopy the diagnosis of patent ductus arteriosus is suggested by a large pulsating and prominent aorta Unfortunately fluoroscopy in the young infant may not be helpful because the thymus overlaps the great vessels so that they are not easily distinguishable A patent ductus arteriosus should be considered if a history of premature birth or of German measles during the first trimester of pregnancy is obtained The pulse pressure is often widened and the diastolic pressure may be

heard down to zero This frequently occurs even when rather severe pulmonary hypertension is present The younger the infant the more difficult it is to accurately determine pulse pressure If the patent ductus arteriosus is an isolated defect, the electrocardiogram is usually normal The electrocardiogram may show left ventricular hypertrophy only or combined right and left ventricular hypertrophy. The finding of right ventricular hypertrophy alone should make one suspicious of an associated ventricular septal defect

The diagnosis is best established by cardiac catheterization Although not pathognomonic, increased oxygen content in the pulmonary artery blood is a helpful diagnostic sign Such a finding occurs also in truncus arteriosus ventricular septal defect and in aortic pulmonic septal defect If the catheter should be passed from the pulmonary artery directly into the descending aorta this is unequivocal evidence of patent ductus arteriosus However, to exclude a common truncus arteriosus, the catheter should be withdrawn to a position in the pulmonary artery The oxygen content of the sample from this position should be lower than it was from the descending aorta If it is not lower than a common truncus arteriosus must be considered In common truncus arteriosus, the pulmonary arteries can rarely be catheterized When pulmonary hypertension, a patent ductus arteriosus, and a pulmonary valvular regurgitation coexist, the oxygen content in the outflow area of the right ventricle is found to be higher than in the right ventricle proper On the other hand increased oxygen content of the right ventricle proper in comparison with right atrium is good evidence of a ventricular septal defect rather than a patent ductus arteriosus A number of patients have been operated upon as ventricular septal defects and found to have, in addition, a patent ductus arteriosus The patent ductus arteriosus had not been suspected clinically from the character of the murmur, the pulse pressure, or any increase in oxygen content in the pulmonary artery In such patients passing the catheter through the ductus has been the only way to establish its presence prior to exploration

The presence of an isolated patent ductus is in itself the indication for ligation and division of the ductus whether or not symptoms exist This attitude is justified because of the low mortality associated with this operation

When both a patent ductus arteriosus and ventricular septal defect are diagnosed preoperatively, there is disagreement as to the procedure of choice In our hospital when a patent ductus arteriosus is found at the time of surgical closure of a ventricular septal defect, the ductus is also divided This has yielded good results, especially when the pulmonary artery pressure is not excessively high Many infants in whom both defects can be demonstrated pre-operatively have balanced pulmonary artery and systemic pressures and clinically show evidence of heart failure, pneumonia and poor growth Rather than wait for a time at which both defects could be closed, we proceed with ligation and division of the patent ductus arteriosus as the first stage Usually patients recover from this procedure rather uneventfully As yet, we have not collected a large series of patients whose ventricular septal defects have been subsequently closed In those patients so managed the risk of closure of the ventricular septal defect should be reduced because of the time interval with decreased pulmonary blood flow and presumably less pulmonary hypertension and secondary pathology When the patent ductus arteriosus is ligated as a first stage procedure, it is important that the pericardium not be opened in attempting to establish the presence and location of any residual intracardiac thrill In patients in whom the pericardium was previously opened, subsequent exploration has been often made more difficult because of obliteration of land marks and of softening of the myocardium If in the future it becomes nearly as safe to perform intracardiac surgery as it presently is to divide a patent ductus arteriosus, the policy of two separate operations should be revaluated We have found that the mortality from cardiac surgery becomes lower when complete correction of the cardiac physiology is attained by the surgery and the patient has normal circulatory hemodynamics to aid his recovery

Patent ductus arteriosus with reversal of flow may represent the final stage of a progres

sive pulmonary resistance secondary to the long continued effects of increased flow and other factors related to production of pulmonary pathology Since some of these patients have been seen and diagnosed under one year of age the question of a primary congenital pulmonary factor has been considered

Regardless of the etiology and pathogenesis the clinical picture varies from the garden variety of patent ductus The history may include failure to grow well pneumonias and exercise intolerance Cyanosis of the legs compared to the arms is usually a later manifestation Generalized cyanosis has been reported

Physical examination may reveal generalized duskiness of the lips finger nails and toenails As the disease progresses the toes become clinically more cyanotic than the upper extremities A rough systolic murmur along the left sternal border is the usual auscultatory finding As these patients are followed a diastolic murmur of pulmonary valvular insufficiency develops due to pulmonary hypertension A diastolic murmur only may be heard later in the course The pulmonary second sound is prominent

The electrocardiogram has invariably shown marked right ventricular hypertrophy The roentgenogram may show a normal or moderately increased size heart The pulmonary artery segment is very prominent The pulmonary vasculature has often been increased suggesting a coexistent left to right shunt The pulmonary vascular markings may merely show large dilated hilar vessels with sparse vessel markings peripherally

The diagnosis may be established at heart catheterization by passing the catheter through the patent ductus and demonstrating desaturation of the femoral artery compared to the right brachial artery There has frequently been evidence of a small increase in oxygen content in the pulmonary artery The pulmonary artery pressures are equal to or greater than the aortic pressures Angiocardiography reveals a dilated pulmonary artery and filling of the descending aorta from the pulmonary trunk and patent ductus

The prognosis for such children has been better than one might expect during the pediatric age range Over all life expectancy however is limited Based on experience in our center and many others the surgical ligation of the patent ductus is contraindicated if the predominant shunt is right to-left If there is a coexistent greater left to right shunt ligation may be undertaken with caution and more reasonable degree of safety

Reversal of flow through a patent ductus has been associated with corrected transposition of the great vessels in several patients This added complication may be suspected when all other diagnostic criteria are present but pulmonary artery segment is not prominent because of its medial position The diagnosis is established by the anterior posterior angiocardiogram outlining the dilated medial pulmonary artery the early filling of the descending aorta and the ascending aorta opacified in later films and forming the left contour of the cardiac silhouette ordinarily occupied by the pulmonary artery

Aortic Pulmonic Septal Defect

This defect consists of a direct communication between the aorta and main pulmonary artery just above the aortic valve The several proved cases seen on our service have presented with a history similar to infants with patent ductus arteriosus or other severe left to right shunt malformations

The auscultatory findings in each patient have been similar to those found in ventricular septal defect When severe pulmonary hypertension has been present a diastolic murmur of pulmonary insufficiency along the left sternal border has been present but this has not been a typical continuous murmur characteristic of the older patient with patent ductus Two of our patients have shown right to left shunting with equal desaturation of the right brachial and femoral arteries

The electrocardiogram under 1 year of age has shown a right ventricular hypertrophy compatible with the age of the patient and definite evidence of left ventricular hypertrophy on the precordial leads The roentgen picture has shown only moderate cardiac enlargement The pulmonary artery segment was prominent in all The pulmonary vasculature and left atrium were prominent in the



Fig 41 Aortic-pulmonic Window Located 5 cm Above the Aortic Valve A The catheter is seen passing through the right side of the heart into the ascending arch of the aorta B Lateral view shows tip of catheter near aortic valve Note the *catheter does not pass into the area of the patent* ductus arteriosus

younger patients One older patient showed normal pulmonary vasculature and no left atrial enlargement

Heart catheterization has been the most decisive method of making the diagnosis There has been a predominant left to right shunt at the pulmonary artery level when pulmonary insuffiency was present increased oxygen content has been present at the ventricular *level in addition* Injection of *isotope in* the pulmonary artery has indicated a right to left shunt by rapid appearance times when *cyanosis was present* The *most diagnostic* finding has been passage of the catheter through the communication and thence into *the ascending aorta* The *first thought* usually has been that the catheter was in a medial descending branch of the pulmonary artery but *rotation of the patient into the* lateral position indicates that this is at the level of the ascending aortic arch (Fig 41) The catheter may pass *from pulmonary artery to* ascending aorta into the right carotid or right subclavian This would almost be impossible through a patent ductus *arteriosus*

Surgical techniques allowing direct vision make closure of this defect feasible The selection of patients for surgery and results should be similar *to those with ventricular de*fects in that the status of the pulmonary pathology (intimal proliferation of arterioles) *may be the most important limiting factor*

For example pulmonary pathology and physiology has been indistinguishable from *primary pulmonary hypertension in one of* our patients and one reported in the literature

Anomalous Coronary Artery Draining into the Right Ventricle

This has been an unusual malformation of *which we have one patient proved at autopsy* and another suspected on the basis of clinical and physiologic data The proven case was a 5 *day old infant* at the time of death The history was that of a loud murmur heard at birth Dyspnea weakness and failure to suck *well prompted early referral* On physical examination the most striking finding was a very loud grade 4 to grade 5 *thrill* and murmur maximum in the xiphoid area This murmur

was a high pitched continuous murmur characterized independently by many examiners as a "buzz saw" or "cutting wood" murmur

The electrocardiogram showed the expected right ventricular hypertrophy compatible with the age but there were striking changes in the ST segments and T waves suggesting myocardial involvement. The roentgenogram showed a large heart, left atrial enlargement and increased pulmonary vasculature. No physiological or angiocardiographic studies were performed. When heart catheterization can be done in such a case the left to right shunt is at the ventricular level and a ruptured sinus of Valsalva or a ventricular septal defect with aortic insufficiency should be considered in the differential diagnosis. The surgical approach has not been explored at our center. Some patients have had no symptoms and surgery has not been contemplated.

Ruptured Sinus of Valsalva

This malformation has classically been considered to be an acquired intracardiac defect but has been recently seen to be a defect present since birth.[34] Of the congenital variety the two more common forms appear to be rupture into the right ventricle (those seen on the pediatric service) and rupture into the right atrium (seen most frequently on the medical service).

In our series of several patients of rupture into the right ventricle the history has been benign and quite similar to a patent ductus or small ventricular septal defect. The physical examination reveals a wide "snapping" pulse pressure. The children are acyanotic. A very loud continuous murmur indistinguishable from a patent ductus arteriosus except for its location of maximum intensity has been present. Our patients have had the murmur described above with the point of maximum intensity to the right of the sternum and lower near the xiphoid process.

The electrocardiogram has shown left ventricular preponderance. The roentgenogram shows a large heart, prominent pulmonary artery segment, left atrial enlargement and increased pulmonary vasculature. The aortic arch is said to be less prominent than in the patent ductus but this has not been constant or helpful in our series.

Diagnosis has been established by cardiac catheterization in which a large left to right shunt has been apparent at the ventricular level. If in the face of such a continuous murmur as described the shunt were found to be at the atrial level the rupture into this chamber is strongly suggested. The pulmonary artery pressures have been only moderately elevated (40 mm Hg) even in the face of tremendous shunts as indicated by heart size and pulmonary vasculature on the roentgenogram.

This malformation has been completely corrected by direct vision intracardiac surgery.

VENTRICULAR SEPTAL DEFECT

This malformation is the most common lesion in our heart catheterization series. With cardiac catheterization being performed on infants this malformation has been diagnosed with increased frequency. These infants may die before the age of one year with this simple malformation. This early death occurs when the ventricular septal defect appears to be an isolated defect or when it is in combination with a patent ductus arteriosus, a mitral stenosis, coarctation of the aorta or an atrial septal defect. Each of these malformations can be potentially cured by surgery.

The history and physical findings are similar to those mentioned above under patent ductus arteriosus. Most show right ventricular hypertrophy alone on the electrocardiogram but a number of patients show right and left ventricular hypertrophy or a left ventricular hypertrophy alone on the electrocardiogram so that this is often not a helpful finding. Presence of high voltage however of both R and S waves across the precordium, the so-called Katz Wachtel[69] phenomenon, has been present in 75% of our patients.[2]

In infants with a ventricular septal defect the roentgenogram shows cardiomegaly, slight to massively enlarged pulmonary artery and right ventricular hypertrophy. The pulmonary vasculature is increased. The finding of large central vessels and normal peripheral vessels suggests pulmonary hypertension

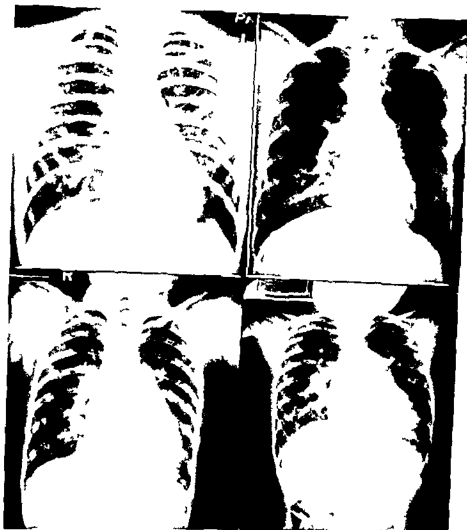


Fig 42 Several Patients With Interventricular Septal Defects A B C and D show increasing size of pulmonary vascular structures associated with increasing size of shunt and pulmonary arterial pressure

Left ventricular hypertrophy is occasionally present If the aorta appears prominent the diagnosis should be questioned (Fig 42)

To establish this diagnosis cardiac catheterization is the procedure of choice Children with clinical difficulty and cardiomegaly will almost invariably have systolic pulmonary hypertension varying from *50* to *100* mm of mercury approaching or balancing with the *systemic pressures We have occasionally catheterized the aorta through the ventricular* septal defect When high right ventricular and pulmonary artery pressures and a large left to right shunt exist the diagnosis of single ventricle should be strongly considered We have seen 1 6 volumes % difference in oxygen content between the right ventricle and femoral artery in cases proven to be single ventricle at necropsy However usually in a single ventricle when the right ventricle and systemic artery samples are taken simultaneously oxygen contents are within a few tenths of each other If the pulmonary artery is not catheterized then a *ventricular septal defect* associated with a common truncus arteriosus *or a corrected transposition of the great vessels* should be strongly considered Since an error is more likely to occur in the clinical diagnosis if the pulmonary artery is not catheterized we obtained in such instances a forward angiocardiogram In the anterior posterior position a corrected transportation of the great vessels

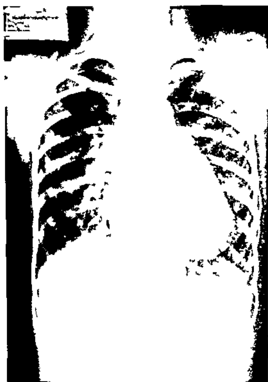


Fig 43 Acyanotic Tetralogy of Fallot (Interventricular Septal Defect with Infundibular Pulmonary Stenosis) in Female Age 6 Years An identical twin sister was normal This roentgenogram shows an increased size of the pulmonary artery hilar structures and a normal sized aorta



Fig 44 Ostium Primum Defect with Small Interventricular Septal Defect in Female Age 2 Years Roentgenogram shows enlargement of undivided pulmonary artery segment and branches The left atrium was slightly enlarged not seen on this projection

will be detected because of the characteristic filling of the aorta near the position usually occupied by the undivided segment of the pulmonary artery In addition the pulmonary artery is medially displaced and the right pulmonary artery is more prominent than usual [47]

Since the life span is definitely limited in patients with ventricular septal defect the treatment of choice is closure of this defect by intracardiac surgery When intracardiac surgery was new the only patients selected were those with the history of repeated attacks of pneumonia heart failure and inability to gain weight The pulmonary artery pressures in these patients were all elevated approaching the systemic levels The mortality was high However an elevated pulmonary pressure alone is not the sole determinate of prognosis from surgery The absence of intimal proliferation in the small pulmonary arterioles is better correlated with survival after surgery These proliferative changes occur in older patients having high pulmonary artery pressures We have however observed patients with severe intimal proliferation at three seven and thirteen months of age who died following surgery In any given individual case there is still no precise physiologic measurement for predicting pulmonary pathology and prognosis at surgery When balanced pulmonary and systemic pressures exist a desaturation of the femoral artery is a contraindication for surgery We have seen no autopsy specimen of the so called Eisenmenger's complex in the pediatric age range which differed in any way in location or size of the defect from our patients with ventricular septal defect who have been successfully closed at surgery It appears that the optimum time to close this defect as an elective

procedure would be over one year of age and with pulmonary artery pressures less than 70% of systemic pressure

VENTRICULAR SEPTAL DEFECT ASSOCIATED WITH MILD INFUNDIBULAR PULMONARY STENOSIS —"ACYANOTIC TETRALOGY OF FALLOT"

Within the past five years we have seen approximately 100 acyanotic patients with a ventricular septal defect associated with infundibular pulmonary stenosis They are usually asymptomatic Some of them are underdeveloped We have seen this malformation in one of identical twins in which growth failure was noticeable This malformation has frequently the loudest systolic murmur heard in any malformation It is usually associated with a thrill of grade IV or V intensity along the left sternal border The pulmonary second sound is not prominent, possibly obscured by the high intensity of the murmur

The electrocardiogram has not been particularly helpful In spite of the presence of pulmonary infundibular stenosis, isolated right ventricular hypertrophy on the electrocardiogram has not been a common finding Some degree of left ventricular hypertrophy is occasionally present This may result from the fact that the portion of the right ventricle subjected to high pressures is small and a large portion of the right ventricle is beyond the area of stenosis where the pressures are normal The roentgen findings are identical with those findings of ventricular septal defect except for a less prominent undivided segment of the pulmonary artery (Fig 43)

At cardiac catheterization the pressures in the pulmonary artery have been normal On withdrawing the catheter through the pulmonary valve, a usual ventricular type pressure is recorded below the valve On continuing to withdraw the catheter through to the tricuspid valve, a high pressure area of 70 to 100 mg of mercury is encountered 1 to 2 cm before reaching the tricuspid valve and atrial pressures. Usually there is an increase in oxygen content of about 1 volume per cent in the outflow area of the right ventricle over the right atrium and the same or a few tenths of a volume per cent higher in the pulmonary artery Unless a pressure tracing is obtained from the pulmonary valve throughout the right ventricle to the tricuspid valve, this diagnosis may be easily overlooked

When cardiomegaly and growth failure exist intracardiac surgery is indicated The ventricular septal defect can be closed and a portion of the infundibulum can be resected Because the infundibular stenosis protects the lungs, these patients are favorable surgical risks

THE OSTIUM PRIMUM SYNDROME

The complete form of persistent atrioventricular canal[16] consists of four major defects first, the ostium primum, or low interatrial septal defect, second, a cleft in the tricuspid valve, third a cleft in the mitral valve, and finally, a small ventricular septal defect underlying the persistent atrioventricular valve This defect occurs embrylogically from the failure of fusion of both left and right tubercles of the dorsal and ventral endocardial cushions Theoretically any one of the four defects mentioned may occur as an isolated malformation However, the ostium primum atrial septal defect and the cleft in the mitral valve commonly occur together, owing to a failure of fusion of the left tubercle of the dorsal and ventral endocardial cushion Failure of fusion of the right tubercle results in a cleft tricuspid valve and a ventricular septal defect. Now the diagnosis of various malformations which include the ostium primum defect can usually be made antemortem

Growth failure frequent pneumonias, heart failure are frequent findings in the history similar to other malformations producing severe left to right shunts Since the median age of survival with this malformation is about 1 year of age, many present with difficulties early in life

Physical findings often include a slight palpable thrill along the left sternal border toward the apex This differentiates it from the usual ostium specundum type of atrial septal defect, but not from ventricular septal defect or patent ductus arteriosus A grade II to III sys-

tolic murmur is usual This is often maximum in the apical area rather than along the left sternal border as in early patent ductus and ventricular septal defect In addition a diastolic murmur is frequently heard along the left sternal border or at the apex

The electrocardiogram is often of great help Most of these patients show a left axis deviation prolonged PR interval a high R in AVL indicating an intermediate or horizontal heart and evidence of right ventricular hypertrophy The evidence for right ventricular hypertrophy may be an RSR' pattern in precordial lead V_1 that is, an incomplete right bundle branch block There may occasionally be left ventricular hypertrophy Although this combination of electrocardiographic changes has been found in 10 to 15% of isolated ventricular septal defects[72] this type of cardiogram should make one strongly suspicious of the diagnosis of the ostium primum type of atrial septal defect

The roentgenography and cardiac fluoroscopy usually reveal cardiomegaly with a very prominent undivided segment of the pulmonary artery Pulmonary vasculature is exaggerated The aorta is small The left atrium may be slightly enlarged usually not to the degree seen with patent ductus arteriosus or ventricular septal defect There may be evidence of left ventricular enlargement on the roentgenogram as shown by failure of the left heart border to clear the spine and the downward slope toward the diaphragm in the left anterior oblique position (Fig 44)

The diagnosis is usually established at heart catheterization by finding a left to right shunt at the atrial level more than normal pulmonary hypertension and most of the clinical electrocardiogram and roentgen findings noted above It has been our experience that there is usually no additional rise in oxygen content at the ventricular level Patients with the ostium primum syndrome ordinarily are fully saturated systemically If pulmonary pressures approach systemic pressures the right atrial pressures may rise producing a right to left shunt at the atrial level and systemic desaturation

This type of malformation is curable by the newer techniques of intracardiac surgery[73] Surgical procedures have been carried out at several centers by closed techniques similar to those used for closure of an atrial septal defect[7, 74] The surgical results with closed techniques were discouraging since the defects were not ordinarily completely closed Direct vision intracardiac surgery is the preferred method However the complication of complete heart block during or following surgery has been higher than in other malformations The over all surgical mortality by intracardiac methods is still discouraging compared to results of closure of ostium secundum type atrial septal defects or isolated ventricular septal defects In the present developmental stage of surgery the good risk patient with no symptoms is ordinarily deferred and the moderate to severe type of patient is selected for surgery

THE OSTIUM SECUNDUM ATRIAL SEPTAL DEFECT

This defect ordinarily occurs in the region of the foramen ovale The opening varies in size The defect may occur near the ostium of the inferior or superior vena cava or near the right pulmonary veins in such a way that partial anomalous pulmonary venous drainage occurs In this latter case the surgeon is usually able to close the atrial septal defect in such a way that the pulmonary veins will drain on the proper side of the septum into the left atrium

In patients with ostium secundum type of atrial septal defect the median age at time of death varies from 19 to 50 years[9] depending on the location of the atrial defect It seems to be quite definite that the majority of cases remain relatively asymptomatic for the earlier part of their life Symptoms and signs do eventually occur handicapping and shortening their lives This may be emphasized by the fact that our series of cases operated upon include twice as many adults as children Only a few children have had clinical symptoms and findings in the pediatric age group which necessitated operation

Less than half of the children fail to grow normally and are tall and thin

Only a soft grade II systolic murmur maxi

mum in the second, third and fourth left interspace is heard. The pulmonary second sound is present and may be only slightly exaggerated. There is no palpable thrill. The finding of a thrill in the pediatric age range should make one suspicious that they are dealing with an atrioventricular canal or some other type of malformation. The pulmonary second sound is often widely split because of the incomplete right bundle branch block and delayed right ventricular contraction.

The electrocardiogram ordinarily shows right axis deviation and right ventricular hypertrophy as indicated by an RSR' pattern in V_1 of the precordial leads, often interpreted as an incomplete right bundle branch block. Cardiac fluoroscopy reveals a heart with slight to moderate cardiac enlargement. The pulmonary artery segment is prominent. The pulmonary vascular markings are exaggerated. The left atrium is not enlarged (Figs. 45 and 46).

The diagnosis is established by finding a difference in the oxygen content of over 1.9 volumes % oxygen content between the vena cava and the right atrium. Ordinarily there is mild or no pulmonary hypertension present in the pediatric age range. One often finds a relative pulmonary valvular stenosis, that is, the pulmonary artery pressure may be 20 mg of mercury when the right ventricular pressure is 30 mg. of mercury systolic.

Several surgical procedures devised to close the interatrial septal defect have average mortality figures from 6 to 8%[3, 4] with good results in about 85 to 90% of patients who survive operation. Direct vision surgery by the use of hypothermia has had a slightly higher recorded mortality rate being in the neighborhood of 10% with good results in 95% of those patients surviving surgery.[75, 6] Direct vision surgery using artificial pump oxygenators is now used. No extensive series has been reported to date.

Indications for surgery would be the presence of growth failure, frequent pulmonary infections, progressive cardiomegaly and progressive pulmonary hypertension. In the older age groups interference with the ability of the patient to attend school or participate in necessary living activities are frequently considered as sufficient handicap to justify surgical closure.

CORRECTED TRANSPOSITION OF THE GREAT VESSELS ASSOCIATED WITH VENTRICULAR SEPTAL DEFECT

Although this malformation has been recognized for years its true incidence and anatomical variations affecting surgery have not been appreciated until recently. Within the last few years we have observed more than 15 such cases.[47] During the same period 150 cases of isolated ventricular septal defects were closed at surgery. This represents an incidence of about 10%. This may be somewhat higher than the true incidence since the condition of these patients deteriorates more rapidly necessitating early referral to our center for surgery. This malformation consists of inversion of the ventricles in such a way that the anatomical right ventricle containing the tricuspid valve and crista supraventricularis lies slightly anterior to the position ordinarily occupied by the left ventricle. The aorta arises anteriorly from this ventricle fullfilling the definition of transposition of the aorta. This aorta ascends along the left border of cardiac contour in the usual location for the undivided pulmonary artery segment simulating this vessel roentgenographically. The pulmonary veins empty into the atrium feeding the ventricle from which the aorta arises so that the patient is fully saturated systemically. The pulmonary artery arises more medially and posteriorly than normal and is fed from the anatomic left ventricle containing the mitral valve and no crista supraventricularis. The physiologic function however is such that the vena cavae empty into the right atrium which feeds the left ventricle which empties into the pulmonary artery.

The history differs in no way from that seen in other fairly severe patients having a left to right intracardiac shunt. The physical findings may give no clue to this added complication of corrected transposition associated with a ventricular septal defect. The murmur and thrill would be located in the usual position.

The electrocardiogram may be helpful. In many instances the PR interval has been pro

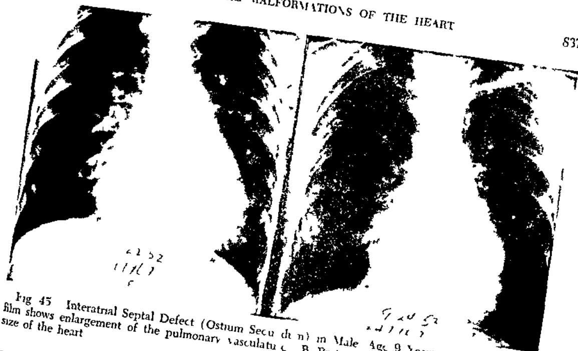


Fig 45 Interatrial Septal Defect (Ostium Secundum) in Male Age 9 Years A Pre operative film shows enlargement of the pulmonary vasculature B Post operative film shows decrease in the size of the heart

Fig 46 Interatrial Septal Defect (Ostium Secundum) in Male Age 8 Years A The roentgenogram shows the enlarged main undivided pulmonary artery segment and the pulmonary artery branches Note the aorta is normal to small in size B The lateral view shows no left atrium characteristic of the ostium secundum defect

longed The finding of a Q wave in V_1 has been usual This is uncommon in other malformations or normal hearts An absence of a Q wave in V_6 is suggestive of corrected trans position The roentgenogram of the heart may be the first clue to this diagnosis. The heart is often moderately enlarged similar to any other ventricular septal defect However, the left main branch of the pulmonary artery appears to arise from a medial position so that the large convex bulge along the left border cannot represent the undivided pul monary artery segment, but actually is the ascending aorta The right hilar pulmonary artery, because of the medial rotation and posterior displacement, is more prominent than the left hilar branch

The cardiac catheterization will indicate a left to right shunt at the ventricular level and a high pulmonary artery pressure Because the right AV valve and pulmonary outflow tract are close to each other in this left ventricle rather than separated as in the right ventricle, the catheter does not usually enter the pulmonary artery If the defect is sus pected, the catheter should be rotated medially and posteriorly to enter the pulmonary artery If the catheter enters the pulmonary artery and films are taken which confirm the medial and posterior outflow tract the diagnosis can be made with confidence An angiocardio gram in the anteroposterior view will show a pulmonary artery filling from a medial position, and when the opaque media returns to the left atrium and "left" ventricle, the ascending aorta will be seen arising on the left cardiac contour in the area ordinarily occupied by the undivided segment of the pulmonary artery (Fig 19)

At the present time the intracardiac closure of ventricular septal defects in this malformation is complicated by the fact that the coronary artery arising from the aorta swings to the right and down between the ventricles in such a way that the right ventricle may not be opened in the usual position to get at the ventricular septal defect without traversing the coronary artery. Other procedures for closing this defect have been considered and an important one with the most promise at the present time appears to be the approach through the right atrium and right AV valve A disturbing finding for us, however, has been the high frequency of balanced pulmonary artery pressures and coincident severe pul monary pathology The findings would appear to put these children into a very high risk category for closure of their ventricular septal defect even if the procedure were well established It would seem that there is strong desirability of being suspicious of this diagnosis, making it as early in life as possible before secondary pulmonary hypertension has advanced to a severe extent

MALFORMATIONS WITH INCREASED PULMONARY FLOW AND SYSTEMIC ARTERY DESATURATION OR CLINICAL CYANOSIS

NON-FUNCTIONING LEFT VENTRICLE SYNDROME

In this malformation the left ventricle is rudimentary secondary to severe aortic stenosis, aortic atresia, mitral atresia or premature closure of foramen ovale The patient usually shows signs of heart failure the first week of life and does not respond well to medical management This group of malfor mations appears to be the most common cause of death due to congenital malformations of the heart in the age group under 1 week

These infants ordinarily will have a low intensity systolic murmur in contrast to the characteristic loud murmur of aortic stenosis in the older age groups The peripheral pulses are often weak and the blood pressures may range between 40 and 50 systolic in the arms and somewhat less in the legs Such a differential blood pressure must not be confused with an operable type of coarctation of the aorta The electrocardiogram usually shows a right ventricular hypertrophy but this would be compatible with the young age of the in fant Roentgenograms of the chest and fluoros copy reveal an enlarged heart, left atrial en-

largement and evidence of congestion and increased pulmonary blood flow The left border may be straight (Fig 47) An angiocardiogram in the left anterior oblique projection or right posterior oblique will reveal an enlarged pulmonary artery and descending aorta filling through a reversing patent ductus arteriosus The ascending aorta is small and often not visible At autopsy the usual findings are a small left side of the heart and a large patent ductus arteriosus connecting directly to the descending aorta The right ventricle is acting as the systemic ventricle The only coronary artery oxygen supply is retrograde through the small aorta from the patent ductus arteriosus

COMPLETE INTERRUPTION OF THE ARCH OF THE AORTA[67]

This malformation consists of a complete separation of the ascending arch of the aorta from the descending aorta at the usual site of coarctation All four of our patients have shown an associated ventricular septal defect and a reversing patent ductus distal to the interruption

History relates difficulty from birth with pneumonitis and/or heart failure Roentgenograms have shown diffuse cardiac enlargement with evidence of pulmonary congestion The physical examination has shown no blood pressure differential between arms and legs or no differential cyanosis of the legs The murmur has been along the left sternal border simulating a ventricular septal defect Femoral arteries have been palpable Elec-

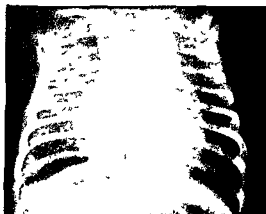


Fig 47 Congenital Mitral and Aortic Atresia with Hypoplastic Left Ventricle in Infant The left border of the heart is slightly straightened The right atrial area is prominent



Fig 48 Complete Interruption of the Aortic Arch with a Reversing Patent Ductus Arteriosus in Male, Age 2 Months This patient had recurring pneumonias and bouts of heart failure A systolic murmur was heard over the [illegible] data indicated a large left to right shunt at th[illegible] desaturated suggesting a single ventricle Th[illegible] artery showed 94% saturation compared to th[illegible] genogram shows large undivided pulmonary artery segment and increased pulmonary vasculature on the right side B Anteroposterior angiocardiogram shows filling of the descending aorta via the pulmonary artery This indicates a reversing patent ductus arteriosus C Retrograde aortogram shows interruption of aortic arch just below left subclavian and proximal to the ductus

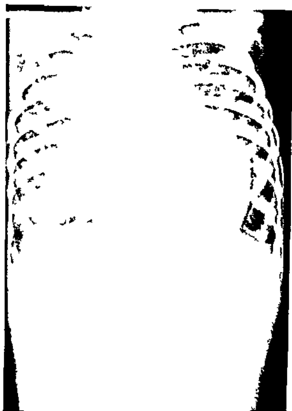


Fig 49 Anomalous Return of the Pulmonary Veins To the Right Atrium With a Patent Foramen Ovale in Male Age 5 Years Minimal cyanosis was present Roentgenogram demonstrates widening bilaterally of the superior mediastinum owing to the dilatation of the left vertical vein and right superior vena cava



Fig 50 Total Anomalous Pulmonary Venous Return into Left Ventrical Vein and Draining into the Superior Vena Cava and Right Atrium A patent foramen ovale was present causing a moderate [illegible] s seen on the posteroanterior roent [illegible] d at this time showed that the left [illegible] ry veins to the left atrium

trocardiogram has shown right ventricular hypertrophy compatible with age

Heart catheterization studies indicated a tremendous oxygen shunt at the ventricular level with the oxygen content similar to the femoral artery oxygen content Systemic pressures in the right ventricle and pulmonary artery suggested single ventricle As far as I am aware single ventricle and complete interruption of the arch of the aorta with ventricular septal defect are the only two malformations in which this may be expected to occur Total pulmonary venous drainage to the right atrium would have similar findings but in addition show high oxygen content in the right atrium

When angiocardiography is done to confirm the diagnosis of single ventricle a reversing patent ductus is seen and no evidence for a single ventricle The diagnosis may then be further confirmed by finding oxygen content differences between the right brachial artery and femoral artery and a retrograde aortogram from the right brachial which shows filling of neck vessels and no opacification of the descending aorta (Fig 48)

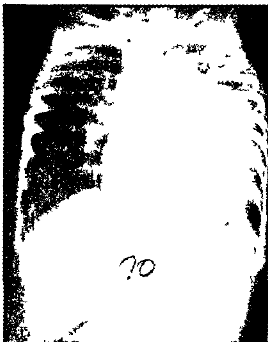


Fig 51 Total Anomalous Pulmonary Return into the Right Atrium Via the Coronary Sinus in Male Age 10 Months Also Foramen Ovale Roentgenogram shows huge right ventricle

TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE TO THE RIGHT ATRIUM[37]

There are four different anatomical variations in this malformation based on the route of drainage into the right atrium When the pulmonary veins join into a common trunk and drain into a persistent left vertical vein and thence to the right superior vena cava the roentgenogram is characteristic the clinical course more compatible with greater longevity When all the pulmonary veins drain into the coronary sinus inferior vena cava or directly into the right atrium the clinical course is more severe and the specific diagnosis of the site of entry more difficult to determine with certainty

The history obtained in patients whose pulmonary veins drain via the left vertical vein into the right superior vena cava often have a benign early history and may be referred because of minimal cyanosis discovered at a few years of age

The physical examination may reveal systemic blood pressure which is on the low side of normal with narrow pulse pressure The femoral arteries are often only weakly palpable The murmur is soft and diffuse The electrocardiogram shows marked right ventricular hypertrophy The roentgenogram shows a characteristic "figure 8" or "hour glass" contour (Figs 49 and 50) The pulmonary vasculature is increased and no left atrium is noted on fluoroscopy The diagnosis is confirmed by catheter studies which reveal a high right superior vena cava and right atrial oxygen content equal to the oxygen content of the systemic artery when these samples are taken simultaneously An angiocardiogram done in the left anterior oblique (RPO) shows opaque media entering the right atrium and going immediately to the left atrium left ventricle and into a normally placed aorta of small caliber The right atrium right ventricle and pulmonary artery are large Pulmonary venous return by the anomalous trunk may be visualized in late



Fig 52 Total Anomalous Pulmonary Venous Return to Right Atrium Via Coronary Sinus with Patent Foramen Ovale A Five years of age roentgenogram shows increased pulmonary vasculature B *Post-operative film shows decreased* pulmonary vasculature compared to pre operative film

films as well as recirculation of opaque media through the pulmonary circuit

If the pulmonary veins connect to the right atrium coronary sinus or inferior vena cava the course has been more difficult and more rapidly fatal Dyspnea and mild cyanosis poor nursing and failure to gain are included in the usual history Physical examination in the young infant reveals a small infant with an active precordium and loud heart tones The murmur is usually not well localized or loud Blood pressures are low and pulses weakly palpable The electrocardiogram shows marked right ventricular activity Left ventricular activity is diminished Negative T waves in V_6 in these instances indicate marked right ventricular activity

The roentgenograms show massive cardiomegaly with a "squared off" "boxy" contour of the left border silhouette (Figs 51 and 52) Pulmonary vasculature is markedly increased No left atrium is noted on barium swallow The presence of definite left atrial enlargement will effectively exclude this diagnosis

The diagnosis may be suspected from angiocardiographic studies which show opaque media moving from a large right atrium to the left atrium and out a small left ventricle and aorta simultaneously with filling of the right ventricle and enlarged pulmonary artery Recirculation through the pulmonary circuit is seen The diagnosis may be confirmed by cardiac catheterization where the finding of high right atrial oxygen content equal to femoral artery oxygen saturation The femoral artery is always desaturated but this may be very near normal values

COMMON TRUNCUS ARTERIOSUS

The common truncus arteriosus types 1 2 and 3 (Edwards)[31] is the malformation of the heart in which only one great vessel arises from the heart This is inevitably associated with a high ventricular septal defect Because the pulmonary arteries arise directly from this trunk the lungs are supplied from a high pressure system resulting in an increased pulmonary blood flow As a result of increased pulmonary blood flow cyanosis is not obvious *there may be several times the amount of* fully oxygenated blood returning to the left ventricle as there is returning from the systemic flow In fact because of a slight degree

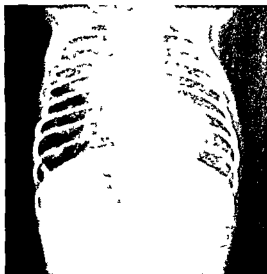






Fig 53 Truncus Arteriosus Type I Female age 3 months A A concavity in the pulmonary artery segment is seen B Angiocardiogram shows the common trunk filling from the right ventricle C Pulmonary artery visualized best by retrograde aortogram

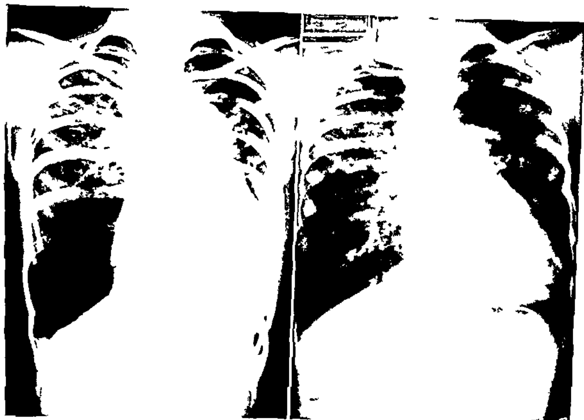


Fig 54 Truncus Arteriosus in Female Age 16 Huge pulmonary arteries are visualized somewhat more cephalad than usual Severe emphysema is seen at both bases A common trunk simulates a large undivided pulmonary artery segment

Fig 55 Truncus Arteriosus in Male Age 8 years A right common trunk is visualized The pulmonary arteries arose from this common trunk

of streaming of blood so that the right ventricular output tends to go in the pulmonary artery and the left ventricular output into the aorta we have seen many patients who have systemic arterial saturations of 91 to 93% and do not appear cyanotic clinically Life expectancy in this malformation is ordinarily quite limited many patients failing to survive the first year of life Some patients have relatively few symptoms with this malformation

The history obtained is similar to other malformations with marked left to right shunting already discussed Unfortunately the physical findings are not distinctive Frequently there is a wide pulse pressure secondary to valvular insufficiency There is often a palpable thrill and loud systolic murmur along the left sternal border The pulmonary second sound is often accentuated and pure without splitting A diastolic murmur may be present and in some patients may simulate a patent ductus arteriosus Most frequently the systolic component along the left sternal border is a prominent murmur and the diastolic murmur is not continuous with it

The electrocardiogram may show either right ventricular hypertrophy or left ventricular hypertrophy no typical findings are present The roentgenograms reveal a heart that is moderately enlarged with a large vessel similar to an ectatic aorta and with no clearly defined main pulmonary artery The area of the chest roentgenogram ordinarily filled with the undivided segment of the pulmonary artery may be concave In some patients there is a convex density in this area simulating the undivided segment of the pulmonary artery In reality it is a composite of the trunk and a dilated left main pulmonary artery posteriorly

located This left main branch often has a higher take off than usual The left atrium is usually enlarged The pulmonary vascular markings indicate excessive pulmonary blood flow (Figs 53A B C 54 and 55)

The cardiac catheterization usually reveals an increase in oxygen content at the ventricular level and an additional increase in oxygen content in the common trunk When the catheter passes into the common trunk an arterial tracing is obtained This is often misinterpreted as being in the pulmonary artery We have found that the pulmonary arteries are very difficult to enter If the catheter is withdrawn to the outflow tract of the right ventricle and opaque media injected the aorta as well as the pulmonary arteries will show simultaneous filling and the nature of the malformation is apparent When the right ventricular blood jets directly into the pulmonary arteries the contrast agent is not sufficiently opaque in the systemic circulation to be seen This is especially true in patients who show slight if any systemic oxygen desaturation In our experience with the forward venous angiocardiogram we have seldom seen opacification of the systemic vessels simultaneously with the pulmonary arteries The high ventricular septal defect the aortic pulmonic window patent ductus and the corrected transposition of the great vessels with ventricular septal defect may at times be confused

At present common truncus arteriosus remains inoperable If it should become technically possible to close the ventricular septal defect so that the trunk is filled from the left ventricle and the pulmonary is transplanted into the right ventricle the operative mortality would remain extremely high because of the advanced state of intrapulmonary vascular pathology

SINGLE VENTRICLE

Single ventricle consists of almost complete absence of the ventricular septum causing obligatory right to left and left to right mixing at the ventricular level both great vessels receiving blood of similar oxygen content Theoretically the femoral artery and ventricular oxygen content will be equal if the samples are taken simultaneously and there is no effect of streaming Although this has been seen it has been unusual to find a single ventricle with normally positioned great vessels More frequently there is some degree of malrotation inversion or transposition of the great vessels The variations may become more confusing when the aorta arises from a rudimentary chamber the pulmonary artery arises from a rudimentary chamber or both great vessels arise from a rudimentary chamber Frequently such a malfunction even at necropsy may be difficult to distinguish from an extremely large ventricular septal defect Diagnosis of single ventricle should be made at necropsy only when one AV valve or both AV valves definitely enter into a single large chamber If there are two AV valves one of which may partially enter a rudimentary chamber and partially a common chamber the diagnosis of single ventricle is less tenable Because of the many variations and relatively few cases seen in each category no clear clinical picture has evolved Life expectancy has been equally variable and many of these children die early in life However some variations of this malformation especially in those associated with pulmonary outflow obstruction have lived 10 years or more In many cases no significant heart murmur may be heard even when there exists definite clinical symptoms and cardiomegaly When murmurs are heard they usually accompany some degree of obstruction in one of the outflow tracts of the ventricles Due to increased pulmonary blood flow these children may not be grossly cyanotic However if the outflow tract of the pulmonary artery has some rudimentary chamber obstruction cyanosis increases with age

In some cases of single ventricle accompanied by a rudimentary chamber from which projects the pulmonary artery superficial characteristics are suggestive of tetralogy of Fallot However it usually seems unlike the tetralogy of Fallot in that the heart is moderately enlarged Also the roentgenograms reveal increased pulmonary vascular markings suggestive of greater than normal pulmonary blood flow hence pulmonary obstruction is not as severe as that seen in the tetralogy of

Fallot. Even with systemic ventricular pressures, heart catheterization will indicate a large left to right shunt at the ventricular level. Often the great vessels cannot be entered and one must establish the diagnosis by finding equal simultaneous systemic pressures in the ventricle and femoral artery as well as equal oxygen contents in both. If the great vessels cannot be entered, injection of opaque media in this ventricular chamber should show simultaneous opacification of both aorta and pulmonary artery and define their relative positions in terms of inversion, malrotation or transposition.

The forward venous angiocardiogram will also show opacification of right and left ventricle and the simultaneous filling of aorta and pulmonary arteries. However, sometimes we have been misled by the fact that forward angiocardiograms seem to indicate first right ventricular filling then left ventricular filling when subsequent necropsy findings showed single ventricle. The reason for this is the tendency for blood to stream such that there is no good evidence of complete mixing.

At present intracardiac surgery is new. If it becomes technically possible for the surgeon to insert a plastic septum dividing the two ventricles partitioning the blood into the proper outflow tracts, pulmonary hypertension and pulmonary arteriolar pathology is likely to cause high mortality from surgery. If outflow obstruction to the right ventricle has been present, surgical intervention may prove effective.

We have seen several patients in which both atrial ventricular valves appear to empty into a large single chamber but actually an anatomical connection does exist between the left AV valve and a small rudimentary ventricle flowing into the aorta. This rudimentary ventricle contains a supraventricular ridge as in the right ventricle and its position is anterior and to the left similar to the aortic position in a corrected transposition. In all aspects this represents a severe degree of corrected transposition of the great vessels. The roentgenogram shows straightening of the left cardiac border and a convexity in the area of the undivided pulmonary artery segment which is in reality the ascending aorta. At catheterization in these cases the pulmonary artery is more frequently entered than in the usual corrected transposition with ventricular septal defect. It is important then to turn the patient in the lateral view to make sure the pulmonary artery arises more posteriorly than normal. In these cases there appears to be a tremendous left to right shunt at the ventricular level even though systemic pressures are evident in the right ventricle. Under such circumstances one should suspect this diagnosis even though there may be a differential in the oxygen content of slightly more than 1 volume % between right ventricular oxygen and that of the femoral artery.

TRANSPOSITION OF THE GREAT VESSELS WITH ATRIAL SEPTAL DEFECT AND/OR PATENT DUCTUS ARTERIOSUS[79]

When transposition of the great vessels accompanies a patent foramen ovale and a patent ductus arteriosus, there are certain findings which distinguish this group of malformations from complete transposition of the great vessels occurring with a ventricular septal defect. The history in both cases is similar. Children are usually mildly cyanotic at birth but become progressively worse. The children frequently do not eat well and their weight gain is less than normal. In transposition without ventricular septal defect the murmur is usually of grade I or II intensity and not well localized. The pulmonary second sound is ordinarily present.

The electrocardiogram shows right axis deviation and right ventricular hypertrophy as evidenced by a high R wave in V_1. However there is very little S wave. The roentgenograms reveal a heart that, if the child is 1 to 2 weeks old, may be normal in size. However the heart enlarges as the child grows and the mediastinum becomes comparatively narrower. The pulmonary artery segment is not prominent. The pulmonary vascular markings are engorged. These sometimes appear to be less engorged when there is only a patent foramen ovale or a patent ductus and more engorged when a ventricular septal defect is associated with transposition of the great

vessels When the infant is less than one month of age the pulmonary markings may appear normal but over the months they become strikingly increased In the left anterior oblique view there is often a widening of the mediastinum (Figs 56 and 57A)

The diagnosis of transposition of the great vessels may be easily confirmed by angiocardiography The opaque media is seen entering the right atrium right ventricle and directly into an anteriorly placed aorta (Fig 57B C). The LAO (RPO) view is the position of choice Ordinarily one does not see contrast agent going into the lung fields returning to the left ventricle and then flowing out the pulmonary artery The outlook is very poor for these children and at the present time there is no curative surgical procedure Medical management of symptoms must be practiced In this malformation several types of palliative heart surgery have been performed This surgery has high mortality and only palliative results[64] However with intracardiac surgery certain procedures have been suggested and may be of real value



Fig 56 Transposition of the Great Vessels in Cyanotic Male Age 6 months Roentgenogram shows a globular enlargement of the heart with narrow superior mediastinal shadow typical of one type of transposition of the great vessels

TRANSPOSITION OF THE GREAT VESSELS WITH VENTRICULAR SEPTAL DEFECT[78]

When this combination of malformations exist the history and physical findings are similar to those mentioned above, except that the systolic murmur heard over the precordium is of grade III intensity and more often localized in the third and fourth left interspace The electrocardiogram may show right axis deviation and right ventricular hypertrophy but more commonly the S wave is deeper all the way across the precordial leads so that neither right or left hypertrophy are suggested on the ECG At present we do not feel there are roentgen diagnostic signs which can clearly delineate the specific type of intracardiac malformation associated with transposition of the great vessels

When definitive heart surgery is available it may be important for the surgeon to know whether a ventricular septal defect is present so that he may plan his procedure accordingly Study is also underway to determine whether severe secondary pulmonary vascular changes appear more commonly and at a younger age in patients who have transposition of the great vessels[66] Preliminary results indicate these secondary pulmonary changes occur more rapidly and with greater severity at a younger age than in simple ventricular septal defects or other malformations This may well be one of the factors limiting the success of surgical procedures

TRANSPOSITION OF THE GREAT VESSELS ASSOCIATED WITH RUDIMENTARY RIGHT VENTRICLE WITH OR WITHOUT TRICUSPID ATRESIA[71]

Eight patients with this malformation have been seen within the past few years in our hospital The history and physical examination are not distinctive from other types of

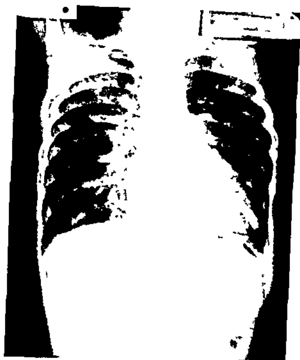




Fig 57 Transposition of the Great Vessels in Extremely Cyanotic Female, Age 2 Years A This shows one type of transposition characterized by an enlarged pulmonary artery segment simulating an interventricular septal defect B and C Angiocardiogram shows aorta filling from right ventricle

transposition. However, frequently these patients will be acyanotic and are dusky only on close examination or as their age increased

The electrocardiogram has ordinarily shown a left axis deviation with peaking of the P waves, absence of right ventricular hypertrophy as measured in V_1 of the precordial leads, and an indication of left hypertrophy on V_6 of the precordials The roentgenogram is identical to the usual picture seen in cases of

transposition of the great vessels The blood pressures have often shown a variance of from 70 or 80 mm in the arms to 40 or 50 mm in the legs However, even with a differential pressure suggesting coarctation of the aorta, there is normal or subnormal pressure in the arms When the blood pressure suggests coarctation, the electrocardiograms suggests tricuspid atresia and the roentgenograms suggests transposition of the great vessels, this entity should be suspected

If one is thinking of this combination of malformations during the interpretation, the diagnosis may be confirmed by angiocardiography in the left anterior oblique (RPO projection) The opaque medium ordinarily enters the right atrium and immediately crosses to the left atrium, left ventricle and fills the pulmonary artery The opaque media may be seen in the aorta which arises anteriorly from a rudimentary chamber or may not be seen opacified at all At present this set of malformations is inoperable These children have been mistakenly sent to surgery for correction of coarctation of the aorta, or for the ligation of a patent ductus arteriosus

Three other anatomical variants have been known to produce identical clinical findings rudimentary right ventricle with transposition of the great vessels without tricuspid atresia, single ventricle, and subaortic stenosis with transposition of the great vessels, and tricuspid atresia with ventricular septal defect without transposition of the great vessels In these cases angiocardiograms may help to separate these entities Transposition of the great vessels with single ventricle has been seen in a few patients These children appear to get along reasonably well and live without undue symptoms or findings for several years In transposition of the great vessels with single ventricle the angiocardiogram shows a simultaneous filling of a pulmonary artery and an anteriorly placed aorta from a common ventricle

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CHAPTER 40

The Heart in Thyroid Disease

C A McKinlay M D

THE HEART IN HYPERTHYROIDISM

INTRODUCTION

The capacity of the thyroid gland to regulate the energy exchange of the body links it intimately with the work of the heart Hyperthyroidism with its increased metabolism is attended by increased minute output of the heart the circulation is physiologically over active Furthermore the cardiac muscle itself as the total protoplasmic mass has augmented metabolism which combined with overwork predicates abnormal myocardial function Contrariwise diminished metabolism of tissues including the heart muscle in myxedema sets up circulatory changes of an other order

The thyroid gland partly on account of its accessibility and partly because of the development of methods of estimating altered function has lent itself effectively to clinical study It is in considerable part through clinical observation that the detrimental influence of hyperthyroidism upon the heart has been recognized and emphasized The effects of hyperthyroidism upon the heart are those due to its overactivity and overwork which appear most striking during the period of aging and concomitant arteriosclerosis Whatever pathological changes have been described in the myocardium in hyperthyroidism have also been noted under other conditions causing heart failure and have not been considered specific or characteristic

The heart in the patient with hyperthyroidism commonly and early responds with tachycardia Increased heart rate as well as blood flow parallels increased metabolic rate Over activity of the sympathetic nervous system mediated through the accellerator fibers to the heart may also be considered an expression of the overload borne by the heart in hyperthyroidism Auricular fibrillation is the most common type of arrhythmia occurring in hyperthyroidism although auricular flutter and A V block have been noted Auricular fibrillation which often first appears in transient episodes tends to become permanent if the provocative hyperthyroidism is not relieved and tends to resist usual therapeutic efforts With persistence of hyperthyroidism into the decades of increasing arteriosclerosis and hypertension the summation of factors including auricular fibrillation causes circulatory inefficiency overwork and heart failure Hypertrophy is not commonly demonstrable but dilatation and increased venous pressure occur with congestive failure The influence of circulatory overwork is better comprehended when it is appreciated that hyperthyroidism may exist over appreciable periods of time Even very moderate overwork existent quite constantly over long periods of time would appear to cause inexorably cardiac overload and to lessen cardiac efficiency There is also quite commonly elevation in the systolic blood pressure and increase in the pulse pressure White states that the true thyrocardiac is the individual who as a result of thyrotoxicosis has auricular fibrillation cardiac enlargement or congestive failure Increasing age makes more probable the development of heart failure Huxthral noted that it

was past 50 years of age that most of the thyrotoxic cases develop heart failure that compensation is usually maintained when regular rhythm is present and that a majority of patients with decompensation show auricular fibrillation

CLINICAL FEATURES OF HYPERTHYROIDISM

Hyperthyroidism is exemplified by the clinical forms of exophthalmic goiter and toxic adenoma Whatever differences may exist between these forms the common factor with regard to the heart is its overactivity and overload In exophthalmic goiter diffuse cellular hyperplasia exists and abnormal eye signs including exophthalmus are commonly present In toxic adenoma the cellular hyperplasia is limited to the adenomatous area or areas The intensity of the hyperthyroidism and rate of development which may be greater in exophthalmic goiter favor greater cardiac overload However toxic adenoma may have insidious onset with delayed recognition and the protracted and total overload may be even greater This is particularly true as the hyperthyroidism of adenomatous goiter often appears in or extends into the age period of degenerative heart disease The writer reported a series of cases of hyperfunctioning adenomatous goiter without tachycardia (above 90 beats per minute) and emphasized the occasional masking of hyperthyroidism by predominating cardiac disturbance

While the appearance of the hyperthyroid patient is sometimes characteristic as in typical exophthalmic goiter in contrast mild or moderate hyperfunctioning adenomatous goiter may give only minimal objective signs The moist oily skin tremors alertness and purposeless movements may be recognized in varying degrees Often forceful and sometimes irregular heart action is complained of and may be the patient s motivation in seeking medical care Altogether the combination of symptoms and signs portrays a syndrome whose early recognition should be emphasized because it may contribute to the prevention of premature heart failure

ONSET AND NATURE OF CARDIAC SYMPTOMS AND SIGNS IN HYPERTHYROIDISM

In the history of the development of hyperthyroidism changes in the emotional and nervous reactions of the individual with unaccounted for weight loss may occur early Such changes are usually associated with early overactivity of the heart with tachycardia Accentuation of heart tones includes increase in the pulmonic second and the first tone at the apex Systolic murmurs may occur but are not distinctive they are more common in the presence of heart failure and have appeared transiently in thyroid crises While the hyperthyroidism varies in intensity and may in certain types of individuals drive them early in the course of the disease to the physician in other patients the process may be indolent over a period of years and may not be recognized until impaired or disturbed cardiac function appears Moreover cyclic variation in intensity of the hyperthyroidism may occur and obscure the evidences of cardiac strain

DIAGNOSIS OF THYROCARDIAC DISEASE

Because the hyperfunctioning goiter is often amenable to surgical treatment its early recognition as a causative or contributing factor in the development of auricular fibrillation and of heart failure is very important The occurrence of auricular fibrillation in a patient with goiter with or without congestive failure unexplained by chronic valvular disease or hypertension or other cause should demand evaluation of the functional status of the thyroid gland Marked increase in its size may not appear It must also be recognized that patients with simple goiters may have preceding or coincident heart disease without clinical significance attached to the thyroid enlargement The occurrence of neurocirculatory asthenia in the patient who happens to have colloid goiter has sometimes led to confusion with hyperthyroidism and useless thyroidectomy has been performed The patient with irritable heart or neurocirculatory asthenia does not show the sustained degree of over

activity and does not have the symptoms of increased metabolism and the quite constant nervous and emotional stimulation characteristic of hyperthyroidism. Cardiac valvular disease, either mitral or aortic, should be recognized by distinctive signs including contour changes. Hypertensive heart disease may be recognized by characteristics of degenerative heart disease, often with electrocardiographic changes of left ventricular strain and demonstrable hypertrophy. Caution must be exercised in interpreting factors such as hypertension by its level during decompensation alone when it may have fallen significantly. The recognition of hyperthyroidism which, though minimal in intensity, is adequate to precipitate cardiac overload, often requires careful diagnostic study. The cardiac manifestations may have become so pronounced that the underlying precipitating cause of hyperthyroidism may be masked more or less effectively. Heart failure developing without adequate cause and non-responsive to treatment should suggest consideration of hyperthyroidism, particularly in patients past 50 years of age.

LABORATORY STUDY

The finding of increased basal metabolism in serial determinations is a valuable adjunct in diagnosis. However, after cardiac decompensation occurs, the elevation of metabolism should not be emphasized until dyspnea and orthopnea have disappeared. Lowered blood cholesterol values are also found in hyperthyroidism. The electrocardiogram gives no specific aid in the diagnosis of heart disease due to hyperthyroidism. Serial electrocardiograms have value in the early delineation of arrhythmia, right or left preponderance depends upon factors primarily independent of hyperthyroidism.

RADIOIODINE IN DIAGNOSIS

During the few years since the report of Hertz, Roberts and Evans, radioiodine (I^{131}) has been frequently used for the diagnosis and treatment of hyperthyroidism. The accepted values of thyroid uptake are now stated to be 15 to 45% of the injected dose 24 hours after administration in the euthyroid, above 45% in the hyperthyroid and below 15% in the hypothyroid according to King. In certain cases of borderline results the test is inadequate. Determination of the protein-bound iodine is becoming an accepted index of thyroid activity. Normal limits vary from 4 to 8 mcgm/100 ml.

PROGNOSIS

Prognosis depends upon variable factors including the age of the patient and the extent of coincident arteriosclerosis and hypertension. Also the longer duration of the process and greater intensity speak for more severe cardiac strain and earlier auricular fibrillation and decompensation. Evaluation of the summation of factors that bring about thyrocardiac disease requires careful study. Assuredly, the longer the duration of auricular fibrillation, the less its chance of alleviation. Hurxthal found that of over 600 operated thyrocardiac patients living over a 21-year period, 28% had auricular fibrillation and that there appeared to be no more deaths among patients who had persistent fibrillation for a long time than for those who had it a short time. Favorable prognosis will be enhanced by brief duration of the hyperthyroidism before its elimination by thyroidectomy or by use of radio-iodine. After return of the metabolism to normal with relief of strain, the ultimate course of cardiac capacity is measured by factors independent of the thyroid disease present in the decades of degenerative vascular disease.

ESSENTIAL HYPERTENSION AND HYPERTHYROIDISM

A moderate increase in systolic blood pressure and pulse pressure occurs in hyperthyroidism. After its alleviation, the blood pressure, associated with the hyperthyroidism, may be expected to fall. However, essential hypertension runs it course independent of intercurrent hyperthyroidism and is usually unabated after thyroidectomy. With associated hypertension and hypertensive heart disease,

the incidental occurrence of hyperthyroidism adds another factor of overwork Relief of the added burden of hyperthyroidism is indicated but does not affect the course of the hypertension in cases personally observed

PREVENTION AND TREATMENT OF THYROCARDIAC DISEASE

Preventive treatment consists in the relief of the hyperthyroidism which if accomplished early in the course of the disease may lessen myocardial excitability and overwork and later obviate heart failure Treatment of the patient with hyperthyroidism in whom heart disease has developed consists in the use of measures to alleviate the hyperthyroidism and to relieve and support the overburdened myocardium In all instances evaluation of the degree of cardiac impairment in the patient should be attempted With the onset of auricular fibrillation and cardiac decompensation, preparation for thyroidectomy should be initiated With persistent auricular fibrillation and appreciable hypertrophy cardiac decompensation may be anticipated earlier Where the cardiac reserve is markedly diminished in older patients in anticipation of possible increase in the life expectancy thyroidectomy after preparation of the patient with iodine may be advised although performed with caution Auricular fibrillation is often refractory to treatment as long as the hyperthyroidism exists with its relief spontaneous return to normal rhythm may occur or response may be obtained from use of digitalis or quinidine The use of rest diuretics and supportive measures for the treatment of congestive heart failure is in order as indicated and completely described elsewhere in the text (see Treatment of Heart Failure)

Cardiac Decompensation Unresponsive to Treatment Until Thyroidectomy

F D female aged 47 single The patient complained of sleeplessness nervousness and heart consciousness There was no important history of previous illness Nine months previously fatigue and dyspnea had appeared followed in about 3 months by cardiac decompensation with edema of the extremities which persisted unabated after hospital treatment digitalis administration and diuretics elsewhere

Examination showed fair nutrition quite marked tremor of hands tachycardia (102) blood pressure 116/96 moderate adenomatous goiter loss of timber of heart tones moderate pitting edema of lower extremities The basal metabolism rate was plus 22 plus 19 and plus 19 % on different dates The electrocardiogram showed only tendency to left axis deviation The diagnosis of hyperfunctioning adenomatous goiter with cardiac overload and decompensation was made The patient was prepared for operation and under Lugol's solution gtts xxx (2 0 cc) daily the basal metabolic rate fell to minus 7 % and the pulse to 78 After thyroidectomy there was improvement in nervous symptoms and relief of dyspnea and edema The basal metabolism dropped to minus 20% and necessitated substitution therapy with thyroid extract Two and one half years postoperatively cardiac compensation was well maintained in this patient at her usual occupation as a teacher

Latent Coronary Insufficiency Made Manifest by Hyperthyroidism

L R B male age 44 married occupation salesman The patient complained of shortness of breath of six months duration provoked by moderate effort slight nocturnal dyspnea at rest and occasional periods of palpitation Increased nervousness of moderate degree had been noted Several attacks of pressure sensation over the precordium with radiation of pain in the left arm were noted for 2 months These had occurred with increasing frequency and were the motivation for seeking medical advice Examination revealed an alert patient and with purposeless movements tachycardia (108) moist skin tremors and small diffuse thyroid enlargement The findings were considered typical of hyperthyroidism and the basal metabolic rate was plus 34 The electrocardiogram was abnormal with low T_1 and T_4 Following thyroidectomy there was recession of symptoms including relief of attacks precordial distress and lessened tachycardia

ence of coronary arteriosclerosis the supervention of hyperthyroidism with its attendant cardiac overwork provoked minimal left heart failure and coronary insufficiency The relief of angina after thyroidectomy and the return of the basal metabolic rate to normal gives support to the above hypothesis The electrocardiographic evi

dence of myocardial abnormality before and after thyroidectomy consistent with coronary insufficiency is also in keeping with the above concepts

RADIOIODINE THERAPY

King states that thyrotoxicosis can be adequately managed by radioiodine therapy and uniform results of 75 to 85% of remissions in treated cases can be expected The procedure has not been used universally in individuals below 35 years of age because of the fear of carcinogenic effects It would now seem that the treatment of choice in hyperthyroidism as related to heart disease may become the use of radioiodine

THYROIDECTOMY

Subtotal thyroidectomy has previous to the development of radioiodine therapy been the treatment of choice for the prompt relief of cardiac overload In the treatment of the nodular goiter and of the firm hard goiter suggestive of malignancy thyroidectomy must be depended upon

In patients of advanced age evaluation in each instance must be made with regard to the hazard of operation and the anticipated increase in life expectancy and alleviation of heart failure In skillful hands thyroidectomy itself presents no special operative risks and has been done in patients with grave degenerative heart disease The preparation for thyroidectomy includes the use of Lugols solution following which there should be quiescence of the symptoms of hyperthyroidism with lessened pulse rate and sometimes alleviation of cardiac decompensation Skill in preoperative handling of the patient a minimum of emotional strain and careful anesthesia reward the surgeon with fewer instances of thyroid crises Thiouracil has been used to reduce hyperthyroidism preoperatively As the benefit from thiouracil is often only temporary sustained alleviation of cardiac overload is hardly to be expected from such therapy The degree of thyroid deficiency is not always predictable Patients who have received thiouracil should have preparation with Lugols solution before thyroidectomy

Following adequate thyroidectomy with lessening of circulatory overload of increased metabolism of the heart muscle and of excitability and restlessness there is increased chance of control of auricular fibrillation This chance is inversely proportional to the duration of the hyperthryoidism which if protracted makes unlikely the resumption of normal rhythm Compensation of the heart is definitely enhanced with relief of its overload and its behavior and ultimate prognosis will then be determined by its freedom from other disease Thyroidectomy should be adequate to assure normal or slightly subnormal function as measured by the basal metabolism Thyroid deficiency if it occurs may be readily controlled by substitution therapy with thyroid extract and is much better for the patient than continuing hyperthyroidism due to inadequate removal of tissue

X RAY THERAPY

While x ray therapy may be used to reduce hyperthyroidism its effect and evaluation thereof extend over a period of some months Such delay and variable results limit the usefulness of x ray therapy in relieving the cardiac overwork and hyperthyroidism In certain instances of recurrent postoperative hyperthyroidism x ray therapy may be given a trial if immediate relief of cardiac disturbance does not appear to be imperative

CONCLUSIONS

The baneful effect of hyperthyroidism upon the heart results from circulatory overactivity and overwork Ultimately arrhythmias including auricular fibrillation and also congestive failure are provoked unless the hyperthyroidism is relieved It is particularly in the decades of degenerative disease that the heart is adversely affected by the overwork of hyperthyroidism The cardiac symptoms may obscure the underlying hyperthyroidism Early treatment may prevent or delay heart failure Radioiodine before or after the onset of heart failure would appear to be the treatment of choice

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THE HEART IN MYXEDEMA

INTRODUCTION

While little has been added to the clinical features of myxedema since their description by Gull in 1874 physiologic variations in the body resulting from deficiency of thyroid hormone remain a matter of great interest The writer s present concern is limited to the effect of hypothyroidism upon the cardiovascular system The symptoms of cardiovascular disease occur not uncommonly in myxedema and have been emphasized and described by Fahr The extent of cardiac disturbances has been variable and depends in part upon the nature and degree of associated cardiovascular disease Symptoms of heart disease were present in 19 of 24 patients who had the clinical picture of myxedema reported by McGavack and others Associated etiological conditions were usually found and consisted chiefly of arteriosclerosis and hypertension Functional disturbances present consisted of right and/or left heart failure and less commonly of angina of effort

CARDIOVASCULAR FUNCTION AND ANATOMICAL CONSIDERATIONS

Deficiency of the thyroid hormone may result in dilatation of the heart although this is more liable to occur when there is associated hypertension or congestive failure The cardiac contour by x ray may show diffuse rather than conus or left ventricular enlargement of mitral stenosis or aortic insufficiency respectively The heart rate is often slow the heart tones may show loss of timber, cardiac output may be low, a systolic murmur is commonly found The electrocardiogram often shows low voltage and sometimes T wave inversions Kern *et al* believe that pericardial effusion is a constant and major factor in the syndrome of myxedema heart That electrocardiographic changes associated with moderate otherwise symptomless hypothyroidism may *occur without pericardial effusion* is illustrated by the case of a 40 year-old woman to be reported by the writer In this instance reversion of distinctly abnormal electrocardiogram to normal was provoked on two occasions by substitution therapy with thyroid extract with normal cardiac contour at all times A recent study reports that the incidence of coronary arteriosclerosis is not greater in patients with myxedema than in euthyroid persons It is of interest that a degree of relative hypothyroidism induced in patients with euthyroid cardiac disease by the use of radioactive iodine has frequently aided in the relief of angina pectoris and congestive failure as reported by Jaffe La Due has reported the autopsy findings in a patient who died of heart failure due to myxedema The heart was globular generally dilated with transverse diameter of 14 5 cm Hydropic vacuolization loss of striation and irregular straining of the muscle fibrils were present but were not considered specific for myxedema heart The heart contour by x ray differs from that of mitral stenosis with its enlarged pulmonary conus and from aortic insufficiency and hypertension with their enlargement of the left ventricle The heart outline is somewhat similar to that in moderate pericardial effusion McGavack *et al* in their cases rarely observed cardiac enlargement in myxedema uncomplicated by hypertension or congestive failure In one patient with severe myxedema and angina of effort the cardiac enlargement was minimal but after substitution therapy with thyroid extract the cardiothoracic ratio dropped from 0.52 to 0 45 These observations suggest that the slight enlarge

ment detected by x-ray would appear to be due to insterstitial edema It appears that the cardiac size varies greatly in myxedema from the marked dilatation associated with congestive failure described in Fahr's first case to that noted above with minimal enlargement

Hallock showed that in myxedema there was reduction of cardiac output and that it was increased by thyroid substitution therapy Physiologic disturbances of the heart in myxedema include definite electrocardiographic changes, the most frequent of which is low voltage of complexes in all leads T wave negativity in Lead I is not uncommon and sometimes is a solitary finding Delayed intraventricular conduction frequently occurs and bundle branch block is not uncommon The electrocardiographic changes due to myxedema itself are reversible with its response to therapy. The frequency in myxedema of other etiologic factors of cardiovascular disease makes desirable procedures for their evaluation. McGavack *et al* from their studies concluded that the blood proteins are of no value in following the results of therapy, that with associated heart failure the variations in weight, basal metabolic rate and circulation time are of no value in determining thyroid status at any particular moment and that an increase in capillary permeability is a constant feature of myxedema, a decrease from the initial high permeability being one of the earliest and most constant signs of improvement The total blood cholesterol usually found to be increased in myxedema has had value in serial determinations in ascertaining the degree of thyroid sufficiency in myxedema with heart failure, for it is uninfluenced by the latter

TREATMENT

The tendency for arteriosclerosis, hypertension and coronary insufficiency to be added factors in heart failure due to myxedema indicates caution in thyroid substitution therapy Particularly in patients with angina of effort or other evidence of coronary insufficiency should substitution therapy be carefully instituted and controlled While the treatment of the cardiac failure takes precedence over that of myxedema, rest, diuretic and digitalis are not completely effective until the myxedema is relieved by substitution therapy If myxedema is the sole etiology, its relief will restore cardiac compensation. The fact that Fahr's first case with severe cardiac failure and marked dilatation did well on an initial dose of 8 grains of thyroid extract daily and in contrast that in two cases McGavack and co-workers had to reduce the dosage to 1/20 grain (05) daily to obviate anginal pain, suggests the variable degree and clinical latency of coronary insufficiency in cases of myxedema with cardiac complications The later observers emphasize gradual augmentation of the dosage of thyroid substance and note satisfactory initial daily doses ranging from 0 05 to 1 grain, with stabilization maintained on 0 5 to 3 grains

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CHAPTER 41

Beriberi Heart Disease

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I INCIDENCE

In the early Seventeenth Century the first European description of beriberi heart disease was written In 1928 beriberi was first reported in this country Beriberi is still most common in the Orient where the polished rice diet is prevalent in this country it is seen and will continue to be seen in endemic form as long as there is chronic alcoholism food faddism and even drug addiction The "wet" type showing peripheral edema, elevated venous pressure, pulmonary congestion and cardiomegally with or without polyneuritis is most common in the middle and far East The "dry or neuritic type of beriberi (occidental) is most common in this country with cardiovascular abnormalities a prominent manifestation Both types however are seen in the United States

II PATHOGENESIS

The relation of oriental to occidental beriberi has been shown that the cardiovascular manifestations are curable with thiamin is well documented Vitamin B_1 present as pyrophosphate or diphosphothiamin functions as a co-enzyme (cocarboxylase) in carbohydrate metabolism The latter is necessary for oxidation of pyruvic acid a derivative of lactic acid and enables utilization of this end product in other metabolic processes In the absence of thiamin pyruvic acid and lactic acid accumulate in the tissues

Beriberi frequently fits the pattern of "high output" type of heart failure Theory has it that the accumulated pyruvic and lactic acids act on the peripheral circulation causing arteriolar and capillary dilatation and therefore causing decreased peripheral resistance This in effect is similar to multiple arterio venous shunts High output failure is the result with typically increased cardiac output rapid circulation time high pulse pressure and "pistol shot" arterial pulsations similar to that seen in anemia A V fistula and hyperthyroidism

Thiamin requirements of the body are determined by the total caloric intake and carbohydrate content of the diet An increase of the dietary carbohydrate therefore predisposes to beriberi or aggravates the disease Experimental animals sustained on diets consisting predominantly of fat and lacking thiamin do not develop beriberi Other conditions such as digestive disturbances psychotic states and those causing increased metabolism such as pregnancy hyperthyroidism exertion and infection may predispose to the disease through poor absorption and utilization or depletion of the vitamin

There are other theories regarding etiology one concerns thiamin deficient metabolism of the overloaded heart and another suggests vagus neuritis as a cause of cardiovascular symtoms Still another pathogenic mechanism of a neurohumeral nature is suggested from work on experimental animals with beriberi where abnormally high concentrations of catecholamines and acetylcholine were demonstrated in the heart

III. CLINICAL PICTURE

There is no rigid clinical syndrome Edema is invariably present with massive anasarca not unusual. Left and right heart failure can both be present although right sided failure with elevated venous pressure and congestive hepatomegaly is most frequent It has been recognized in the Orient that individuals with thiamin deficiency who perform hard physical labor develop cardiac and circulatory failure but frequently do not display polyneuritis Neck vein distention rapid circulation time and "pistol shot" phenomena have been mentioned Dyspnea and orthopnea are variable depending on the degree of pulmonary congestion The pulse is usually rapid and blood pressure is either normal or elevated with typically high pulse pressure In spite of pulmonary congestion pleural effusion is infrequently found Cardiac murmurs are variable and heart tones are usually of poor quality Electrocardiographic changes are non diagnostic T wave lowering or negativity and decreased QRS voltage is most common ST lowering has been reported Characteristically conduction defects do not frequently occur, although experimentally *bundle branch block* has been produced in thiamin deficient animals

With treatment response is frequently dramatic Case reports where thiamin was used along with bed rest and low salt diet but without digitalis or mercurial diuretics show rapid recovery One series of cases displayed arterial hypertension as the outstanding clinical feature during recovery If treated early enough in the course of the disease with adequate amounts of thiamin the individual should have complete recovery with no predeliction to recurrent or other types of heart disease

IV DIAGNOSIS

Blankenhorn's criteria for diagnosis are widely accepted They are (1) enlarged heart with sinus rhythm (2) dependent edema (3) elevated venous pressure (4) peripheral neuritis or pellagra (5) non specific changes in the electrocardiogram (6) no other cause evident, (7) gross deficiency of diet for three months or more (8) improvement and reduction of heart size after specific treatment or autopsy findings consistent with beriberi

A response to low salt diet mercurial diuretics bed rest and digitalis does not however preclude the diagnosis of beriberi heart disease

V TREATMENT

The response to therapy is variable dependent upon severity and duration of the disease Thiamin is given in doses of 100 mg daily with diet not excessive in carbohydrate because of the proved detrimental effect Bed rest and salt restrictions are important and occasionally mercurial diuretics and digitalis are necessary It is significant that in some reported cases these latter measures alone do not give recovery Coexistent vitamin deficiencies anemia and infectious states are treated as they occur In the properly treated early case diuresis occurs in the first 24 to 48 hours Reduction in heart size reaches a maximum in 2 to 3 weeks with electrocardiographic changes reversing in 2 to 4 weeks

VI PATHOLOGICAL FINDINGS

The heart at autopsy is usually enlarged and may be normal or increased in weight Characteristically interstitial and perivascular edema and separation of muscle fibers is evident and less frequently hydropic degeneration is present In oriental cases enormous

right sided dilatation with myocardial degeneration and fibrosis has been reported This is uncommon in the occidental form Isolated cases of focal necrosis and subendocardial fibrosis have been reported It is noteworthy that although these changes are characteristic they are non specific

VII. PROGNOSIS

Griffith has studied in detail the end results of acute beriberi in 109 Americans held prisoners of war by the Japanese during World War II These individuals survived the effects of beriberi and severe malnutrition for 44 months He concluded that patients who survive the acute stages of beriberi and are afforded proper treatment do not have residual cardiac damage clinically and have no predeliction to cardiovascular diseases of other causes He concluded also that inadequate treatment can be the cause of protracted or recurrent heart failure late in the disease and that there may be persistent subclinical microscopic myocardial changes

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CHAPTER 42

Cor Pulmonale

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Cor pulmonale may be defined as hypertrophy and dilatation of the right side of the heart with or without signs of congestive failure secondary to diffuse pulmonary disease. Pulmonary hypertension is the major physiologic derangement responsible for the structural changes in the heart. Not all cases of right heart failure secondary to pulmonary hypertension can be considered as cor pulmonale since pulmonary hypertension developing as a consequence of left ventricular failure, mitral valve disease, or congenital heart disease is excluded by definition.

ETIOLOGY

Acute cor pulmonale may occur as a result of a more or less sudden occlusion of a significant portion of the pulmonary vasculature resulting in an acute rise of pulmonary artery pressure. Pulmonary embolism following peripheral venous thrombosis is the most common cause of this phenomenon. Fat embolism following extensive fractures has also been implicated. The right ventricle is essentially a bellows type of pump designed to move a relatively large volume of blood against a low head of pressure. Such a pump cannot adapt well to sudden increases in pressure, and in the case of the right ventricle acute dilatation and failure may occur as a result of the pulmonary hypertension secondary to pulmonary artery embolization.

Chronic pulmonary hypertension and chronic cor pulmonale are often the result of the interplay of three different factors: (1) abnormal relationships between alveolar ventilation and perfusion, (2) impaired alveolar capillary diffusion of oxygen, and (3) a decreased pulmonary vascular bed. Chronic diffuse obstructive pulmonary emphysema, the most common cause of cor pulmonale, is a good example of a disorder which disrupts normal alveolar ventilation perfusion relationships. It occurs as primary pulmonary emphysema or may develop as a consequence of chronic bronchitis and fibrosis in bronchiectasis, severe asthma of long duration, and kyphoscoliosis associated with poor ventilatory function and impaired bronchial cleansing. Other etiologic agents in the genesis of this form of emphysema include extensive pulmonary tuberculosis with fibrosis, sarcoidosis associated with peribronchiolar or endobronchial lesions, pneumoconioses, and fungus infections.

Impaired diffusion of oxygen across the capillary alveolar membrane is produced by the granulomatoses of sarcoid and beryllium and by the interstitial fibrosis seen in the Hamman Rich syndrome, pulmonary asbestosis, scleroderma, and silicosis. Alveolar cell carcinomas and the lymphatic spread of other neoplasms also produce diffusion barriers.

Lesions involving the pulmonary vessels with the production of pulmonary hypertension may be either intraluminal or extraluminal. The blood vessel changes found in pulmonary hypertension include medial hypertrophy and arteritis obliterans, necrotizing arteriolitis, and pulmonary atherosclerosis. The intimal lesions secondary to long sustained pulmonary hypertension tend to produce further increases in pressure and thus are part of a vicious cycle. Chronic pulmonary hypertension can follow repeated pulmonary embolization often with organization and recanalization. Extraluminal lesions, either granulomas or fibrosis, may

diminish the size of the vascular bed significantly Actual thrombosis of some of the vessels may occur and they may also be lost by replacement of areas of necrosis with scarring The rupture of interalveolar septa in emphysema can lead to a true loss of vessels as well as the loss due to compression of the tissues surrounding the blebs Regardless of the cause if the total cross sectional area of the vascular bed is sufficiently reduced pulmonary hypertension leading to cor pulmonale can result

Chronic massive thrombosis of either main branch of the pulmonary artery or even of the main pulmonary artery itself is a much less common cause of cor pulmonale Occlusion of only one main branch of the artery must be associated with reduction in functional reserve of the opposite lung before cor pulmonale will develop

With the exception of a few cases of cor pulmonale due to pulmonary arterial changes alone as in primary pulmonary hypertension all three of the factors mentioned above may be present in a given case of chronic cor pulmonale but the effects of any one may be predominant

PATHOLOGIC PHYSIOLOGY

One of the functional abnormalities in chronic diffuse obstructive emphysema is the uneven distribution of respired gases which upsets normal ventilation perfusion relationships Diminished ventilation of perfused alveoli produces anoxia and hypercapnea since the perfusion of such areas constitutes in effect a pulmonary arterio venous shunt The hypoxic stimulus exerts a direct effect upon the pulmonary vasculature resulting in an increased vascular resistance which in turn is manifested as pulmonary hypertension The exact site of the pulmonary vasoconstriction is not known Hypoxia is also a stimulus for increasing the cardiac output which may remain high despite right heart failure Increased red cell production leading to polycythemia is another compensatory mechanism initiated by hypoxia The hypervolemia which accompanies it results from an increased red cell mass rather than an increase in plasma volume The plasma volume may be normal Both the high cardiac output induced by hypoxia and the increased viscosity of the blood due to the polycythemia are additional factors in the genesis of the pulmonary hypertension Another consequence of the disturbed ventilation perfusion relationships is the tendency to retain carbon dioxide This ultimately is followed by more or less irreversible loss of sensitivity of the respiratory center to this substance

As the disease progresses other forms of intrapulmonary shunting may occur as well as that associated with perfusion of non ventilated tissue Pre capillary anastomoses between bronchial arteries and pulmonary arteries have been demonstrated in animals and probably are present in man in diseased states Such anastomoses could contribute to the development of pulmonary hypertension Other anastomotic channels include those between the bronchopulmonary and the pulmonary veins The normal flow in these anastomoses is from the pulmonary to the bronchopulmonary veins emptying ultimately into the azygos system In chronic cor pulmonale with right heart failure the valves at the entrance of the bronchopulmonary veins into the azygos may become incompetent and a reversal of flow may occur contributing to systemic arterial desaturation

When a diffusion barrier (capillary alveolar block) is the predominant physiologic disturbance hypoxia may be apparent only during exercise early in the disease Alveolar oxygen tension is normal The cardiac output may be somewhat elevated initially but ultimately the vessels in the interalveolar septa may be reduced in number by the disease and the cardiac output then falls Since carbon dioxide is much more diffusable than oxygen respiratory acidosis is not a part of capillary alveolar block and in fact carbon dioxide values may be normal or low because of hyperventilation

In chronic cor pulmonale associated primarily with pulmonary vascular obstruction and with a reduction in size of the vascular bed the cardiac output is usually normal or low in the compensated state and tends to fall when failure develops Hypoxia is not a prominent feature in these cases unless shunt

ing occurs either as mentioned above or through a patent foramen ovale The cyanosis sometimes observed in these patients may be the result of capillary stasis rather than arterial desaturation

Chronic cor pulmonale initiated by anoxia and without pre-existing pulmonary disease occurs in people who live for many years at very high altitudes When the atmospheric pressure falls to the point where alveolar oxygen tension is reduced and arterial desaturation exists adaptive changes including an increased cardiac output and polycythemia occur However pulmonary hypertension also develops Both pulmonary and cardiac compensation may be maintained for many years When compensatory mechanisms begin to fail carbon dioxide retention develops as in other cases of cor pulmonale and right heart failure appears The symptoms and the physiological abnormalities are reversible by moving to lower altitudes

SYMPTOMS

The symptoms of chronic cor pulmonale are primarily those of pulmonary insufficiency including dyspnea tachypnea cough and wheezing The cough may be productive of purulent and tenacious sputum Recurrent lower respiratory tract infections are common Chest pain from pulmonary hypertension resembles that of angina pectoris and occurs with exertion Nitroglycerin does not usually relieve it It is more commonly seen in primary pulmonary hypertension than in secondary pulmonary hypertension Syncope occurs with primary pulmonary hypertension sudden death has been reported The carbon dioxide retention which may be associated with advanced pulmonary disease leads to mental confusion somnolence or coma The appearance of right heart failure is associated with right upper quadrant abdominal pain due to hepatic engorgement ascites and dependent edema as well as accentuation of the pulmonary symptoms There is an increased incidence of peptic ulcer in patients with chronic cor pulmonale this should always be considered when abdominal pain is one of the symptoms

DIAGNOSIS

A diagnosis of chronic cor pulmonale may be entertained whenever right ventricular hypertrophy or enlargement or signs of right heart failure are found in a patient with bilateral diffuse pulmonary disease or with disease involving the pulmonary vessels Chronic diffuse obstructive pulmonary emphysema must be differentiated from senile emphysema without significant functional impairment Positive physical findings include cyanosis tachypnea and other evidences of pulmonary disease such as fixation of the chest and diaphragm decreased breath sounds wheezes rales and rhonchi Although right ventricular overactivity and accentuation of the pulmonic second sound may be present they are not always detectable because pulmonary emphysema may mask the underlying changes Evidences of right heart failure occur in advanced disease and may be intermittent coinciding with acute respiratory infections Arrhythmias are uncommon in chronic cor pulmonale pleural effusion is relatively rare

Chest films will reveal dilatation of the pulmonary artery increased pulmonary vascular markings and right ventricular enlargement as well as changes in the pulmonary parenchyma Rapid attenuation or pruning of the pulmonary vascular markings toward the periphery of the lungs is very suggestive of pulmonary hypertension Films of the chest taken after expiration are helpful in detecting localized areas of emphysema when these are due to endobronchial lesions The usual films obtained after inspiration will not always reveal the full extent of the disease Chronic massive thrombosis of the pulmonary artery as a cause of cor pulmonale may be suspected when radiographic examination reveals a striking decrease in the pulmonary vascular markings as well as increased radiolucency of the lung fields It is almost impossible to make an accurate correlation between the radiographic appearance of the lungs and the extent of functional impairment EKG changes include right bundle branch block and the findings of right ventricular hypertrophy Abnormally tall or peaked P waves are also seen Pulmonary function tests are of value in evaluating ventilatory or diffusion abnormalities

TREATMENT

In patients with chronic diffuse obstructive pulmonary emphysema every effort should be made to improve ventilation and relieve airway obstruction The margin of reserve is very narrow in these patients and the involvement of only small amounts of additional lung tissue can make an appreciable difference clinically Respiratory infections such as pneumonia or acute bronchitis must be vigorously treated An acute respiratory infection is often the precipitating factor in heart failure in patients with chronic cor pulmonale since it may lead to an increase in anoxia and an increase in pulmonary hypertension as well as carbon dioxide retention Acute congestive failure in such circumstances may respond promptly to treatment of the infection alone Many of these changes are partially reversible at least temporarily

An element of bronchospasm is present in a high percentage of patients with obstructive emphysemas It should be treated with dilator drugs such as aminophylline and ephedrine (either alone or in combination) If necessary more potent agents such as isoproterenol (Isuprel) may be used Thick tenacious sputum obstructs airways and is difficult for the patient to expectorate Adequate hydration is essential for the reduction of viscosity of these secretions as a valuable adjunct saturated solution of potassium iodide begun in an initial dose of 5 drops three times a day and increased to 15 drops three times a day will result in a less tenacious sputum Liquefying agents with detergent properties (such as Alevaire) administered by nebulization sometimes are useful Antibiotics are indicated for the control of infection In addition to the unquestioned effectiveness of the more potent antibiotics the place of sulfonamide preparations such as sulfisoxazole (Gantrisin) should not be overlooked Long term antibiotic therapy presents some hazards overgrowths of resistant bacteria or fungi in the lungs may be more serious than the original disease The antibiotics are therefore best given in relatively short courses

Polycythemia in chronic cor pulmonale may eventually reach a point where it is no longer compensatory Because of the increased viscosity of the blood it actually impairs cardiac function Phlebotomy may be indicated, but must be approached more cautiously than in the patient with primary polycythemia. The hematocrit is the best guide for this form of therapy It should not be reduced below the level of fifty Hypercapnia is best treated by measures directed toward improving alveolar ventilation The use of acetazoleamide (Diamox) a carbonic anhydrase inhibitor has been advocated because of its effect in promoting the renal excretion of bicarbonate The response of an individual patient to this drug is not always predictable or sustained It may lead to an increase in acidosis Its effectiveness in reducing carbon dioxide retention or arterial pCO_2 through direct action has not been proved. Some of its beneficial effect may be secondary to the diuresis that it induces the secondary reduction in thoracic blood volume may facilitate more effective ventilation and removal of CO

Oxygen often appears to be necessary in the management of patients but may lead to severe hypercapnea with coma and death because of loss of sensitivity of the respiratory center to the stimulus of carbon dioxide The respiratory center is controlled by chemoreceptors which will respond to change in oxygen tension of the arterial blood The carbon dioxide content of the blood may be kept within relatively normal limits by the hyperventilation secondary to anoxia but although the administration of high concentrations of oxygen may correct the unsaturation, it tends to depress ventilation and in this way leads to further accumulation of carbon dioxide and narcosis Oxygen when necessary must therefore be administered in a relatively low concentration and only under close supervision Patients who are critically ill may require a respirator to insure adequate ventilation particularly if oxygen is required for severe anoxia Narcotics are contraindicated and sedation with other drugs must be used with the utmost caution because of the possibility of respiratory depression

Digitalization is indicated whenever cardiac failure is present and maintenance doses should be continued indefinitely The argu

ment that digitalis should not be used in those cases with high cardiac outputs is not valid Other measures for the treatment of failure such as diuretics and sodium restriction are important

When one of the major problems in chronic cor pulmonale is capillary-alveolar block with a diffusion defect, as in certain cases of sarcoid, ACTH, cortisone, or meticorten may be of value The nature of the response is not always predictable, and in a few patients an increase in fibrosis and rapid deterioration seem to occur

There is no satisfactory treatment for disease involving the pulmonary vasculature itself as in primary pulmonary hypertension or in pulmonary hypertension secondary to repeated showers of small emboli Anti hypertensive medications are without benefit

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CHAPTER 43

Heart Disease and Pregnancy: General Physiologic Considerations

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PREGNANCY consists of the formation from the smallest beginnings of a new life for which the mother must provide a shelter within the uterus, the building materials for growth, oxygen and fuel for a fabulously busy construction process. All this puts increasing demands on the mother throughout pregnancy. To these processes should be added alterations in the tissues which make the improbable act of childbirth relatively simple. Finally there is the preparation for lactation. On the circulation of the mother falls the brunt of these new demands. During the vast proliferation of growing cells the total maternal and fetal mass grows proportionately to the oxygen consumption which increases about 20%. There is much less increase in basal metabolic rate. Whenever metabolism increases, the increased demand on the heart is met in a number of ways. For brief demands the pulse rate speeds up and the output per beat as well as the output per minute may both increase. In the slowly rising new demands of pregnancy the heart progressively increases its output from about the twelfth to about the thirtieth week, by which time cardiac output is roughly 40% above normal. In the last 8 or so weeks of pregnancy this progressive rise ceases and during the last month there may be an actual fall from the highest level. Most of the increase in cardiac output results from an increased stroke volume but some results from a quickening of the pulse which increases on the average 15 beats per minute. The circulation is faster and not as much oxygen is abstracted as the blood goes through the tissues. Thus the arteriovenous oxygen difference is diminished. The increase in cardiac output is greater than the rise in consumption of oxygen. Since the peripheral resistance is not increased and may even be reduced, the increase in cardiac output is a fairly accurate reflection of the increase in work load on the heart. The speed of the circulating blood accelerates so that the circulation time is diminished. This decrease in circulation time is already apparent by the third lunar month and has reached its peak before the tenth lunar month, so that during the last 4 to 5 weeks of pregnancy the speed diminishes slightly. Part of the new circulatory requirement for the growing fetus is made up by an increase in blood volume. This increase is not equally distributed between plasma and red cells. The plasma volume increases roughly 40%—the red cell mass roughly 20%, so that a state of hypervolemia may occur. The red count, which measures cells per unit rather than total cell mass, declines somewhat. Most of these changes have reached their peak some 4 to 5 weeks before delivery. For reasons altogether obscure a reversal in this trend occurs during the last month of pregnancy. In sodium retention an increase in total body water may be noted. Presumably these are related to steroid hormone changes, though in what proportion estrogens, aldosterone and other adrenocortical steroids are important is not yet settled. These alterations may continue up to the time of delivery.

Venous pressure in pregnancy rises in association with increase in blood volume and increased venous return. Venous pressure has

been found to be notably high in the legs This has been assumed to be a result of the encroachment of the uterus in the pelvis on the veins draining the lower extremities Infra red photographs however demonstrate an increase in the size of the veins before the uterus is large enough to obstruct or significantly impede the movement of venous blood upward through the pelvis by compression of the pelvic veins and inferior vena cava This change occurs at a time when veins over the breasts and upper chest are experiencing a similar engorgement Here no simple pressure mechanism can be invoked There is some evidence that opening of arteriovenous aneurysms in the lower extremities and elsewhere may be associated with the varicosities of pregnancy To what extent later compression of the inferior vena cava by the uterus may contribute to varicose veins in the legs and to congestion of the kidneys and albuminuria is not settled but it certainly may be important

Electrocardiographic changes in pregnancy include various ectopic beats prominent S wave in Lead 1 and a conspicuous Q wave and an inverted T wave in Lead 3 because of rotation of the heart and its displacement upward Frequently there is a left axis deviation Occasionally a deep Q-3 is encountered presumably also a result of changes in position of the heart The findings in vectocardiography appear to be related to similar positional changes in the heart These normal changes must be recognized in looking for electrocardiographic evidence of heart disease in pregnant women

CLINICAL CHANGES DURING PREGNANCY

The various changes in the stress put on the circulation during pregnancy are partly mechanical partly humoral and partly metabolic Certain normal changes take place regularly as the uterus increases in size so as to begin to displace abdominal and thoracic contents upward The heart is pushed up into the left side and somewhat forward as pregnancy progresses giving an apparent increase in its transverse diameter approaching or exceeding the usual ratio of 50% of the thorax This must be distinguished from true cardiac enlargement Such displacements may give a false impression of indentation of the barium filled esophagus suggesting mitral valve disease Sometime around the beginning of the third lunar month of pregnancy the blood volume begins to increase This reaches its peak about the seventh or eighth month and then it declines slowly until term A feeling of fullness and tension may go far beyond what is expected from the pressures and stretchings in pelvis and abdomen Plasma volume expands somewhat more than does red cell volume This causes a hypervolumic state suggesting anemia Observations of Ferris and Wilkins and Burwell indicate that the placenta may act as an arteriovenous fistula with the maternal circulation resembling that in peripheral arterio venous fistula Some of the changes may begin well before the placental circulation has assumed a volume adequate to explain these changes so other factors may operate and the analogy is by no means complete

Alteration in steroid hormone metabolism with changes in sodium and water occur It is generally agreed that water retention is a feature of normal pregnancy Cardiovascular changes late in pregnancy may result from an increase in volume and tortuosity of the placental villi which raises the resistance to blood flow

Paralleling the increase in blood volume there is an increase in cardiac output during pregnancy though many observations reveal that it becomes established several weeks later than the first indication of increasing blood volume Its maximal level is reached between the twenty sixth and thirty second week and after this time it falls gradually although ordinarily it is still somewhat elevated at the end of pregnancy Values indicating an increased cardiac output of 25 to 50% have been obtained

Examination of the heart may reveal extra systoles systolic murmurs and increase in loudness of the heart sounds particularly the

first sound at the apex and the pulmonic closure sound at the base Presumably these are caused by mechanical factors and increased cardiac activity The normal third heart sound may increase in loudness or be heard for the first time The elevated diaphragm may encroach on the lungs and rales may be heard at the bases Recent observations suggest that pulmonary arteriovenous shunts may appear during pregnancy or latent ones become functional during pregnancy Oxygen consumption which begins to rise during the second lunar month continues to increase slowly during the whole pregnancy very much in proportion to the increase in size of the uterus and its contents Observations that serum iodine remains constant during pregnancy suggests that the increase in oxygen consumption is not the result of overactivity of thyroid hormone and a manifestation of mild thyrotoxicosis but rather that the increased volume of tissue requires increased oxygen supply

Certain symptoms occur in perfectly normal pregnancy These symptoms may be much exaggerated during pregnancy in women with heart disease While many of the symptoms are aggravated or precipitated by emotional forces there is a sound physiologic basis for many of them Shortness of breath particularly as pregnancy advances a repeated sighing efforts to get a deep breath and annoyance with the process of breathing may occur With a reduction in ventilation and vital capacity the usual mechanisms for dyspnea may exist Sometimes the increased effort required to get enough oxygen is not properly adjusted to the need Hyperventilation may develop in such circumstances Palpitation and fast pulse are frequent and with the hyperkinetic state of the circulation throbbing warm extremities palpitations extrasystoles and arrhythmias with some tachycardia may increase the symptoms Edema of the lower extremities particularly later on in pregnancy, may add to the general distress The heart displaced upward and outward may beat rather forcefully against the chest wall so that palpitation is common even in normal pregnancy

SUMMARY OF CARDIOVASCULAR ADAPTATIONS OF PREGNANCY

Changes in cardiac output blood volume velocity of blood flow blood viscosity and hematocrit which occur during pregnancy continue in such a way that the resultant circulatory burden increases slowly in early pregnancy rapidly from the fifth month until the maximal level is reached during the ninth lunar month at which time there begins a dramatic turn towards normal during the final weeks of pregnancy This restitution towards normality continues rather rapidly but not precipitously after labor Thus what formerly seemed to be a logical belief that the circulatory "load" in pregnancy increased steadily throughout the entire period of pregnancy is shown not to be correct Though the exact mechanism by which the circulatory burden is relieved during the last phases of pregnancy is not known it is very important to be aware that such indeed is the fact since it is an important landfall in treating a patient with congestive heart failure during pregnancy A respite can be expected well in advance of the actual termination of pregnancy The major alterations in circulation during normal pregnancy are elevation in blood volume cardiac output and oxygen consumption which is increased relatively less than cardiac output and is associated with a decrease in arteriovenous oxygen difference Increased velocity of blood flow increased pulse pressure and heart rate with a diminution in hemoglobin content red cell count hematocrit and blood viscosity per unit volume of circulating blood are further characteristics Some of these circulatory changes in pregnant women resemble those in patients with arteriovenous fistulas They have in common increased cardiac output blood volume pulse pressure pulse rate venous pressure in nearby veins and decrease in arteriovenous oxygen difference and a continuous bruit with systolic accentuation to be heard over the aneurysm or the uterus These physiologic alterations of

the circulation which has to carry on much more business during pregnancy seem to be perfectly adequate to explain the reason why congestive failure may be precipitated in a person with heart disease if pregnancy occurs Other things being constant the earlier heart failure appears in pregnancy and the more severe it is the worse the outlook

Vital capacity decreases during pregnancy but very few studies have been made with the newer methods of studying pulmonary function and to what extent mechanical intrusion of abdominal contents into the thorax congestion of the vascular spaces in the lung or other factors contribute is not known

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Soon after delivery there may be a rather sudden and as yet unexplained diminution in blood volume and then toward the end of the first day when this decline has stopped diuresis begins the slow process of shrinking the blood volume Observations of palmar erythema and vascular spiders in pregnancy though having no direct bearing on heart disease suggest that humoral factors must be operating which produce changes in the small blood vessels not only in the skin of the palms and the upper portion of the body where spiders occur but throughout internal organs of the body in addition to uterus and placenta The exact mechanisms of these changes are not known but it is strongly suggested that steroid hormones particular estrogens are related to the process Lactation keeps some of the increased circulatory demands alive but on a much smaller scale

HEART DISEASE IN PREGNANCY

GENERAL COMMENTS

The kind of heart diseases which occur during pregnancy are those to which younger persons in the prime of life are particularly liable For most purposes heart disease of pregnancy is rheumatic heart disease It accounts for at least 90% of the cases the remainder being distributed amongst congenital heart disease hypertensive heart disease, and certain rare causes of trouble such as thyroid disorders dissecting aneurysm syphilis and bacterial endocarditis Studies from various parts of the world suggest that between 1 to 2% of pregnant women have heart disease This proportion may increase as a new group of women survives operations on deformed or diseased hearts

Another aspect of the problem is the occurrence of heart disease arising because of pregnancy Essentially this is hypertension connected with pregnancy in ways not yet clear At the present time cardiac disease is a cause of maternal death ranging next to hemorrhage and toxemia

A properly functioning cardiovascular system is essential to the smooth running of normal pregnancy which in itself subjects the circulatory apparatus of normal women to a burden by no means completely understood Better understanding of cardiac function and

a shift in the incidence of various cardiac diseases in pregnancy are going on simultaneously. It is fortunate that our understanding of circulation in normal states and in nonpregnant women has provided us with a better basis upon which to study the circulation in pregnancy. Likewise the great number of operations done on the heart in children and young women has brought into the childbearing age a substantial number of young women formerly doomed as invalids, spinsters or childless wives who are now eligible for marriage and pregnancy. It is not so often the bleak duty of a physician to inform a young woman that because she has a bad heart it would be dangerous or suicidal for her to have children. Active studies in several parts of the world have attacked the problems of circulation in pregnancy and the hazards of heart disease in pregnant women. Nevertheless it has taken about 25 years for much of the early confusion to be cleared away. It is hoped that the future will see still more important advances.

The formidable contribution of heart disease to both maternal and fetal death once loomed fairly large. Heart disease added an inevitable toll in pregnancy and pregnancy added its hazard to heart disease. But also there was much traditional error in treatment, a lore based on little understanding and much misunderstanding of the problems. Notable in this regard was the frequency with which intervention by the physician spoiled the pregnancy and added another danger to the patient's life. In the light of present knowledge interruption of pregnancy is rarer and the time can be chosen on more rational grounds.

CLINICAL ASPECTS

Heart disease and pregnancy may be associated in a great many different ways. (1) A person whose heart disease is known may become pregnant whether she be advised to do so by her physician or warned against it. (2) Pregnancy may be the precipitating cause of congestive heart failure in a patient whose heart disease was asymptomatic or not recognized. (3) Pregnancy itself may precipitate heart failure through the derangements associated with hypertension and toxemia. (4) Structural changes in the connective tissue matrix of the body in pregnancy occasionally favor the development of dissecting aneurysm. (5) Similar changes may favor the rupture of the aorta in pregnant women who have coarctation. (6) Of course heart failure may occur in a pregnant woman for reasons completely independent of pregnancy as in an intercurrent bout of rheumatic fever or the excessively rare case of myocardial infarction. (7) From another point of view pathologic states in the mother may damage the growing fetus and produce congenital cardiac deformities. A classical example of this is found clinically in the various deformities which may arise when German measles occurs in a woman during the first trimester of pregnancy. By analogy with experimental animals and in the light of the work of Warkany and others specific dietary deficiencies occurring at critical times during the formation and growth of an embryo may produce midline fusion deformities, congenital cardiac anomalies and a host of other lesions. These latter groups are mentioned merely for inclusiveness and will not be discussed.

The general physician, obstetrician or internist may encounter heart failure in pregnancy as a sudden emergency in a woman whose health has been excellent and in whom heart disease has not been recognized. It may occur as an anticipated risk in a woman whose heart disease is well established clinically. It may occur as a true medical emergency with acute left ventricular failure and pulmonary edema which requires speedy measures to take the strain off the engorged venous system and right heart. Or it may develop slowly in the face of early symptoms recognized for what they are and despite appropriate therapy.

The first thing is to be sure that one is dealing with actual congestive failure and not merely an exaggerated example of the physiologic changes of pregnancy. This should not be too difficult and a history provides the best method of getting evidence on this point. But since dyspnea and edema may both occur in normal pregnancy one has to be careful in assessing their importance. When the picture is full blown with elevated venous pressure

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Hypertension may occur in pregnancy Pregnancy may occur in a person with hypertension though as a general rule women with severe hypertension are somewhat less likely to become pregnant than those without it On the other hand hypertension may be extremely severe and pregnancy occur Leaving out coarctation surgically correctible unilateral renal disease and pheochromocytoma the acquired hypertension of pregnancy is a disease of obscure origin It may be extreme or mild or intermediate Usually it disappears soon after the interruption or natural termination of pregnancy The incidence of hypertension in pregnancy seems to be diminishing in clinics *where it is being studied intensively* probably because of more attention to such matters as salt restriction and general hygiene during the prenatal period The approach to hypertension during pregnancy should begin with such simple procedures as rest in bed and restriction of salt These may be all that are necessary If the condition is serious or progressing however it may be necessary to use proveratrine or other drugs which lower the blood pressure in order to prevent convulsions and to permit pregnancy to continue If in spite of all proper medical measures it is still not possible to control the blood pressure or congestive failure the interruption of pregnancy should be considered but not until such measures have failed and the clinical situation is deteriorating

TREATMENT PREVENTION, CURE, PALLIATION

It is a shocking experience for a young woman in the bloom of youth to be told that she must not have a child because she has heart disease Fortunately physicians are not nearly so often the bearers of such dark tidings as was true even as recently as three decades ago One of the encouraging developments of the scientific approach to medicine has been the realization that much of the fear of pregnancy in women with heart disease was unfounded or grossly exaggerated It may be laid down as a general rule that women who have heart disease which interferes with their normal activities should not have children Whether this end is to be obtained by celibacy, continence or contraception one should look upon wilful pregnancy as little short of suicidal despite the fact that an occasional woman gets away with it But many persons who have had some signs and symptoms of heart failure can get through a pregnancy with wise precautions and careful continual attention to common sense rules of hygiene and appropriate medical therapy Such patients rarely present difficulties but it is those whose trouble arises *de novo* or who have disregarded advice where difficulties crop up The major consideration in treating heart trouble in those who are pregnant should be directed at the heart itself Pregnancy itself can be more or less forgotten At least it must not be interfered with on the grounds of heart failure Thus one can lay down the general law that under no circumstances should pregnancy be tampered with in a patient who has congestive heart failure until all medical measures for treating heart failure have been exhausted Naturally one is uneasy when he sees a pregnant patient in the throes of desperate congestive failure

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HEART FAILURE AND CONGENITAL HEART DISEASE

Espino Vela and Castor Abreu have reviewed medical writings on congenital heart disease complicated by pregnancy and their own experience with a large number of cases A person with congenital heart disease will want to know these things before undertaking pregnancy (1) Is the condition surgically correctible or curable and if so when is the optimal time for doing the operation? (2) What is the added risk of a congenital heart ion in pregnancy and the added risk of ancy in someone with congenital heart e? (3) What is the likelihood if any e child might have a similar or related nital deformity? Just as with acquired disease notably mitral stenosis the de of tolerance to exercise and general ac ty which a patient has had before preg ncy is a reasonable measure of what may anticipated in pregnancy If the symptoms have been minimal pregnancy is likely to go along uneventfully If however congestive failure has occurred or exercise tolerance is severely limited one may anticipate a certain amount of difficulty In general the severity of the lesion will bear a relationship to the prognosis A person with a very wide open patent ductus can look for much more trouble than a person with a hemodynamically small or inconsequential, one To some extent a person with patent ductus arteriosus runs into the hemodynamic handicap of a second arteriovenous fistula represented by the full development of the placenta the enlargement and vascularization of the uterus and the growth of the fetus In atrial septal defects an overloading of the right side of the circulation in association with pregnancy may lead to a reversal of the direction of the shunt and its unhappy sequels Coarctation which interposes a special barrier to the circulation of the blood in the pelvis and lower body may lead to some reduced fertility in women as it sometimes does to impotence in men It is a serious risk in pregnancy though many women with coarctation have survived normal pregnancies Part of this worse prognosis results from the handicap of added circulatory

strain and part from the increased risk of dissecting aneurysm Pregnancy itself is not a contraindication for surgery though it is by no means the time of election for doing correcting operations on the heart and great vessels Bacterial endocarditis remains one of the extra hazards and in spite of theoretically excellent therapy occasionally the outcome of bacterial endocarditis in pregnancy is not good The risk of bacterial endocarditis or endarteritis in a patent ductus calls for prophylaxis and consideration of the advisability of operations before pregnancy

HYPERTENSION

Hypertension may occur in pregnancy Pregnancy may occur in a person with hypertension *though as a general rule women with* severe hypertension are somewhat less likely *to become pregnant than those without it* On the other hand hypertension may be extremely *severe and pregnancy occur* Leaving out coarctation surgically correctible unilateral *renal disease and pheochromocytoma* the acquired hypertension of pregnancy is a disease of obscure origin It may be extreme or mild or intermediate Usually it disappears soon after the interruption or natural termination of pregnancy The incidence of hypertension in pregnancy seems to be diminishing in clinics where it is being studied intensively probably because of more attention to such *matters as salt restriction and general hygiene* during the prenatal period The approach to *hypertension during pregnancy should begin* with such simple procedures as rest in bed *and restriction of salt These may be all that* are necessary If the condition is serious or progressing however it may be necessary to use protoveratrine or other drugs which lower the blood pressure in order to prevent convulsions and to permit pregnancy to continue If in spite of all proper medical measures it is still not possible to control the blood pressure or congestive failure the interruption of pregnancy should be considered but not until such measures have failed and the clinical situation is deteriorating

TREATMENT PREVENTION, CURE, PALLIATION

It is a shocking experience for a young woman in the bloom of youth to be told that she must not have a *child because she has* heart disease Fortunately physicians are not nearly so often the bearers of such dark tidings as was true even as recently as three decades ago One of the encouraging developments of the scientific approach to medicine has been the realization that much of the fear of pregnancy in women with heart disease was unfounded or grossly exaggerated It may be laid down as a general rule that women who have heart disease which interferes with their normal activities should not have children Whether this end is to be obtained by celibacy continence or contraception one should look upon wilful pregnancy as little short of suicidal despite the fact that an occasional woman gets away with it But many persons who have had some signs and *symptoms of heart failure can get through a* pregnancy with wise precautions and careful *continual attention to common sense rules of* hygiene and appropriate medical therapy *Such patients rarely present* difficulties but it is those whose trouble arises *de novo* or who have disregarded advice where difficulties crop up The major consideration in treating heart trouble in those who are pregnant should be directed at the heart itself Pregnancy itself can be more or less forgotten At least it must not be interfered with on the grounds of heart failure Thus one can lay down the general law that under no circumstances should pregnancy be tampered with in a patient who has congestive heart failure until all medical measures for treating heart failure have been exhausted Naturally one is uneasy when he sees a pregnant patient in the throes of desperate congestive failure

But scrupulous and devoted nursing care rest in bed the employment of digitalis diuretics and salt restriction sometimes with oxygen occasionally emergency phlebotomy and thoracentesis are remarkably effective remedies Treatment must be guided by close medical attention with reassurance judicious employment of sedatives and an optimistic attitude Whether or not an operation should be done needs to be evaluated on the basis of individualizing the problem As a general rule pregnancy itself rarely constitutes a contraindication to the surgical correction of a deformed valve or a congenital or acquired lesion If the pregnancy is interrupted it should be done electively in the first trimester Even elective abortion is a sign someone has failed be it patient or physician If pregnancy has gone on beyond this time in most instances it is best to let it go Cesarean section has no place in the treatment of such patients unless there are other reasons for doing it Remembering that the last month is likely to be "on the downhill slope" if not coasting all the way, should enable the physician to convey his charge to the proper harbor without radical futile and dangerous intervention

The strains which pregnancy puts on the circulation are comparable to those of a pilgrim beginning a long journey in the flat and easy lowlands The way becomes steeper and more troublesome very difficult near the end of the ninth lunar month when the path rises to a peak Suddenly almost a month before journey's end and unexpectedly the summit has been passed Though the altitude is still high the road slopes downward Then at the appointed time of labor there is another sharp rise but a brief one Thereafter the way passes into the golden promised land with pulmonary embolism or other accident presently only a rare tragedy lurking unexpectedly

CONDUCT OF LABOR

In a person with heart disease labor should be as expeditious as possible This means careful attention to the heart and letting nature take its course as far as delivery is concerned This is more important when there is congestive failure Respect for the physiologic urgencies of orthopnea must be kept in mind and the recumbent position must not be enforced especially during anesthesia

PROGNOSIS

The average prognosis for persons with heart disease who become pregnant can be estimated fairly satisfactorily from various classifications such as that of the American Heart Association and the New York Heart Association Thus there are several series of reports of patients in Class I definite organic disease but no limitation of activity with no maternal deaths Class II organic heart disease with slight or moderate limitation of activity deaths may occur but are extremely rare In Class III those with moderate to great limitation of activity deaths may be expected in approximately 5% In Class IV those who might be looked upon as actual cardiac invalids or persons who are severely incapacitated have an extremely bad outlook Death in about 30 up to 50% of those who become pregnant Women who fall into this latter category have a tendency to sterility and a considerable increase in early abortions and spontaneous miscarriages as though Nature were trying to prevent or correct the difficulty added by the pregnancy Additional individual factors to be kept in mind are that a bad prognosis is to be anticipated in women (1) who have auricular fibrillation (2) who have had congestive failure (3) who have hypertension (4) who are relatively old for pregnancy that is in the middle or late 30s or older They have about twice the chance of getting into difficulty that the younger pregnant cardiac has (5) who have had acute rheumatic fever (6) who have

miscellaneous complications which add the handicap of a serious disease in their own right such as syphilis diabetes tuberculosis and other conditions

THE EFFECT OF PREGNANCY ON HEART DISEASE

A question which comes up from time to time concerns the possible deleterious effect of pregnancy on heart disease Whether or not congestive failure occurs the concensus of opinion is that if the person survives pregnancy and makes a normal recovery no measurable worsening in the heart disease is likely to be detected A bout of congestive heart failure if it lasts for a long time may add insult to injury and thus make the condition worse though it is impossible to dissect out such other factors as the mere passage of time which other things being the same brings the cardiac patient nearer to his final doom The importance of such conditions is not yet separable in weighing the many factors which go into the prognosis and survival in heart disease Formerly it was considered that pregnancy always produced a permanent increase in cardiac disability in a person with heart disease but we know now that this does not occur

It is important to remember that pregnancy is a very good test of the circulation In a person with rheumatic heart disease the knowledge that several pregnancies have come and gone uneventfully indicates good cardiac reserve at least at the time of the pregnancies

POSTPARTAL FAILURE

Women without previous sign of heart failure who have gone through a clinically normal pregnancy sometimes develop congestive heart failure in the weeks following delivery There is doubt as to the significance of such an event—is the pregnancy simply coincidental or is there some as yet unknown factor by which pregnancy or the puerperium itself damage the heart and cause it to fail? Toxic infectious and endocrine mechanisms have been postulated to explain the clinical course of sometimes intractable congestive failure Nonspecific myocarditis fibrosis and scarring may be found at autopsy Though it is amply demonstrated that postpartal heart failure occurs it is probable that many examples of the clinical condition are cases of known kinds of heart disease which happen to occur in women late in pregnancy or after delivery Certainly the cardiac burdens of pregnancy and their brisk but brief exacerbation at delivery are gone during the puerperium The heart which fails after pregnancy can hardly be reacting as it were to an afterthought of prior damage Much more study with modern methods and critiques is needed before we accept as an entity congestive failure which assails women when the troubles with pregnancy should be over Nevertheless the time of delivery and the easement of the puerperium confer no exemption from heart failure of any kind commonplace or obscure

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General Comments

The remarkable strides on our knowledge of pregnancy and heart disease are illustrated by comparing the information in Sir James Mackenzie's book on Heart Disease published in 1921 with that of Jensen in 1938 and that of Hamilton and Thompson in 1941 to which of course a considerable advance has been added by the studies done in numerous clinics with newer methods for evaluating circulation In Mackenzie's time very little could be suggested except the termination of pregnancy where failure and pregnancy occurred together It is to a large degree the result of work in Hamilton's clinic that we now have a more enlightened view of when heart disease exists or occurs in a pregnant woman The three most important textbooks are

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CHAPTER 44

Rare Diseases of the Cardiovascular System

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"Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path, nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the unusual law of nature by careful investigation of cases of rarer forms of disease

—WILLIAM HARVEY

THE HEART suffers failure and ultimate ruin from coronary artery disease and its attendant damage to muscle, from the strains caused by hypertension and from deformity of the valves with leaks or obstructions Patients who suffer from such disorders constitute the bulk of those whose damaged hearts ultimately fail in their function and thus finally cause death It is hoped that wider familiarity with such diseases eventually will lead to a better understanding of their cause, their nature, their cure and ultimate eradication For the present we get small solace from the recognition of diseases where diagnosis merely enables us to know that the prognosis is very bad and treatment most often frustratingly ineffectual

Our understanding of the natural history of the common heart diseases is fairly well advanced Ordinarily we can recognize the problem when a patient with heart failure does not fit into one of the classical or well defined groups While interest in the rare forms of heart disease is very old, it could not be of much help to the physician until the commoner entities were studied and understood For about 20 years, active interest in uncommon diseases has led to a much better understanding of such rare diseases and syndromes and new ones are being described from time to time or old ones rediscovered I have discussed reasons for emphasis on rare diseases because understanding any disease process is valuable in the advance of medicine In the aggregate, the patients with various rare diseases of the heart bulk large They constitute an important element among patients with all forms of cardiac diseases, though no one physician's experience with any single rare disease is likely to be very large Some of the mysterious neglect of rare diseases of the heart was removed in 1939 when Soma Weiss wrote a very important paper on "Diseases of the heart and the aorta which are not well recognized" In the same year von Bonsdorff contributed a series of papers on the same general topic These articles and many written subsequently have gone a long way toward making such diseases well recognized

This section makes no attempt to be all inclusive Even books on rare forms of heart diseases have been selective Some diseases, such as beriberi, have become nearly extinct while others such as the syndrome of metastatic carcinoid seem to spring up all around us Though the mechanism by which the heart is hurt in some rare diseases is not known most of the trouble is heart muscle failure Unhappily for many of the victims of these diseases the treatment is as ineffectual as the pathogenesis is obscure

MARFAN'S SYNDROME-AN INBORN FAILURE OF CONNECTIVE TISSUE

Marfan's syndrome, arachnodactyly or dolichostenomelia, is a disease of myriad masquerades It might be taken as the textbook illustration of the multitudinous ways in which a genetically determined dysplasia can deform any part of the cardiovascular system and then destroy the patient Almost any system of the body may be implicated and persons with Marfan's syndrome have sought help in all major medical specialties The condition was first described by Marfan in 1896 but only in the last two decades has the disease become familiar to American physicians Very obvious physical deformity makes the diagnosis easy if the condition is known Different stigmata may occur singly or in any combination Parents with only the ocular manifestations may transmit the tendency which affects viscera in an offspring, or a child with ocular lesions may have a parent with only skeletal changes Typically the patient is thin, cadaverous in appearance, with sharp prominence of the bones, and conspicuous deficiency of fat and subcutaneous tissue The height is usually greater than normal and the span of the outstretched arms is longer than the height This may result from artifact because of spinal curvature Many different skeletal deformities develop in older patients where the scanty ligamentous and muscle support have proved inadequate for stability of the bony framework Joints, especially those of the hands and feet, are remarkably pliable though the hyper flexibility may later give way to contractures From the long sinuous fingers, resembling as they do a spider, the name "arachnodactyly" or spider fingers is derived The toes and arches of the feet may be cramped and out of alignment The bones have no organic defect but they may warp, or be deficient in substance which leads to spina bifida, cranial bosses, calcaneal spurs, pigeon breast or pectus excavatum A great variety of congenital cardiovascular lesions have been reported and a number of lesions may be acquired later in life Atypical lung formation may be associated with peculiar liability to pulmonary disease In addition to displaced lenses, the pupils may be refractory to mydriatics Tremulousness of the iris, and cataracts are not unusual These pariahs of nature are able to lead a surprisingly normal life, and mental capacity is not impaired ordinarily As freaks, they may have focused upon themselves much unwanted attention Some of the victims of the disease capitalize on their monstrosities and gravitate to the freak collection of the circus and side show where they are on display as the "living skeleton" or the "thin man" Death is likely to occur in the 30's or the 40's, but very mild cases live longer

The cardiovascular anomalies of Marfan's syndrome may fall into several different categories Those of the heart itself include atrial septal defects and the tetralogy of Fallot There may be anomalies of the valve, lengthening, sacculation and rupture of the aortic cusps, bacterial endocarditis, and conduction defects Occasionally the skeletal deformities with extreme pigeon breast or pectus excavatum may lead to pulmonocardiac failure The aorta may be the site of dissecting aneurysm with or without fusiform aneurysm of the ascending aorta, dilatation of the aortic ring, and more rarely coarctation or patent ductus arteriosus The degree of coarctation is rarely of clinical significance The pulmonary artery may have aneurysmal dilatation or dissection Emphasis on atrial and occasionally interventricular septal defects in the early writings on this subject probably gave a false impression of their frequency Recent reports would suggest they are much less common than such disasters as dissecting aneurysm Patients with Marfan's syndrome should be studied for possible congenital cardiovascular defects and patients with various congenital cardiovascular defects should be evaluated for the possibility that they or their families might have Marfan's syndrome Midline fusion defects and tetralogy of Fallot are cases in point The valves, particularly the aortic and mitral valves, may have a variety of deformities Bacterial endocarditis may settle on a valve diseased by the processes of Marfan's syndrome Clubbing of the long gracile fingers in arachnodactyly presents a remarkable clinical picture Conduction defects are in no way specific Most of the arrhyth-

mias have been encountered in patients with Marfan's syndrome The electrocardiogram may be perfectly normal

Lesions of the aorta are most extensive in the media with fragmentation and rarefaction of the elastic fibers and dissolution of internal elastic membrane Gaps between the fragmented fibers are filled by ground substance which is vaculated and seems to be edematous There is breaking up and degeneration of collagen fibers Focal edema basophilia of the ground substance various degenerative changes in the muscular portions of the media with the characteristic liquefaction of the medial necrosis of Erdenheim may be seen With the constant pounding of the throbbing intravascular forces on the aortic wall slow weakening of media may lead to fusiform aneurysm with or without subsequent dissecting hematoma of its wall In fact fusiform or localized aneurysmal dilatation of the aortic wall is one of the commonest of the cardiovascular anomalies associated with Marfan's syndrome Deformity of the valve ring with sacculation aneurysmal distortion of the sinuses of Valsalva and anomalies of the valve cusps occasionally may cause fenestration or rupture Diastolic murmurs some loud enough to be heard at a distance from the chest may add to the diagnostic confusion[8]

Minimal changes which occur in the aorta and the resulting dissecting aneurysm are exactly the same as those of Erdheim's cystic medial necrosis The late changes consist of disruption of the elastic lamella and the dissolution of the hyperplastic and enlarged smooth muscle fibers of the media into a disorganized conglomerate jell interlaced with greatly dilated vascular channels and small aneurysmal vessels coming in from the adventitia It is not known whether vascular changes lead to asphyxia death degeneration of the media, or whether the elastic fibers degenerate first leaves the smooth muscle without its proper stabilizing support so that abnormal action leads to a raveling contracture of muscle fiber which has lost its proper attachments and stability Whether the process is primarily vascular and nutritional or primarily degenerative with decaying elastic fiber effectively putting smooth muscle cell out of business the end result is complete structural disorganization Sometimes there is slow weakening of the wall diffusely sometimes it is disorganized abruptly by a dissecting hematoma arising from one of the distorted aneurysmal vasa vasorum coming in from the adventitia

McKusick's observations indicate that approximately 15% of cases of Marfan's syndrome occur sporadically without any other member of the family being affected Once the disease arises it is transmitted as a mendelian dominant The only effective therapy is prevention This can be applied only to known victims of the disease since it is rarely fatal before the childbearing period is well along Treatment of each individual lesion from aneurysm to dissecting aneurysm to congenital valve disease to bacterial endocarditis is the same as for other examples of such disorders based on the commoner forms of preexisting disease It would appear that surgical attack on the aorta for fusiform or dissecting aneurysm would probably be somewhat less likely to succeed than in patients whose disease was more localized since most of the tubing is made of very weak tissue in Marfan's syndrome

DISSECTING ANEURYSM

In the spectrum of clinical examples of dissecting hemorrhage hematoma or aneurysm of the aorta there is overlap of many conditions some common some rare Dissecting hematoma of the aorta arises from any pathologic process which produces sufficient weakness and structural disorganization of the aorta to permit necrosis and degeneration of the media and a rupture of small vasa vasorum producing a hemorrhage which may dissect along the cleavage lines of the media separating the inner and outer coats in the form of a glove or cuff This may extend far down branching vessels or may stop short of the first branch The process may be minute or massive If the dissection is extensive it may ac

tually cut off the blood supply which normally flows through different branches of the aorta This may be seen where dissection envelops the mouths of coronary vessels, renal vessels and others, giving rise to varied symptoms which depend on what structures have local ischemia produced by the impinging pressures of the shearing action of the encroaching blood The aneurysm may rupture through the adventitia, filling the pericardium, pleural spaces, peritoneal cavity or tissue spaces with blood It may rupture back into the lumen of the aorta which then permits the transmission of the high intra-aortic pressures to extend the splitting dissection In an occasional patient the dissection may not put any vascular segment out of commission enough to kill If the patient survives, blood may flow through both channels of an inner and outer aortic passage way, or if the dissection has not encircled the aorta, it may develop a gun barrel, two lumen tube with surprisingly little inconvenience to the rare victim who outlasts the early stages

The antemortem diagnosis of dissecting aneurysm of the aorta was quite rare until the researches of Shennan were published in a monograph which is still the classical source of information about this interesting disorder Actually it had been identified more than 200 years earlier and its pathology was fairly well worked out more than a hundred years ago Still it was looked upon as a curiosity, a topic for pathologists, but of no consequence for the clinician since a characteristic train of signs and symptoms was not appreciated Thus it lingered under the vast clinical neglect of mysterious disease until the last two decades Now it is a favorite diagnosis of junior medical students and a perennial booby trap for those who make the CPC circuits

Among the things which can damage the media and provide fertile grounds for dissecting aneurysm, hypertension with arteriosclerosis is the commonest Here the media is damaged by two processes One, the continual hammering of the high intravascular pressure, and two, lesions in the vasa vasorum themselves produce ischemia and ultimately asphyxia and cell death Weakening of the muscular and elastic support of the media follows Another form, existing independently of hypertension, is called the idiopathic medionecrosis of Erdheim Some light has been cast on this situation by Ponseti and his coworkers who have demonstrated that growing rats fed a diet high in sweet pea meal have high risk of developing dissecting aneurysm as well as kyphoscoliosis, hernias, and a general disorder of the connecting substances which glue together the tissues of the body Persons with idiopathic kyphoscoliosis have an increased risk of developing dissecting aneurysm [18] Experimentally, any condition which damages the media, whether it be experimental atherosclerosis, scurvy, surgically induced ischemia, or mechanical stripping may give rise to dissecting aneurysm Dissecting aneurysm is fairly common in coarctation but here the mechanical integrity of the vessel is disrupted by the structural deformity of the congenital anomaly, perhaps abetted by hypertension In addition to idiopathic kyphoscoliosis, there is an added risk of dissecting aneurysm with normal pregnancy, presumably because of the general softening of the connective tissue matrix associated with advancing pregnancy This not only makes ready the genital passages for delivery of the child but is manifest by softening and relaxation of ligaments and connective tissue generally The myxomatous alterations in myxedema provide another rarer background for dissecting aneurysm Finally hamsters treated with cortisone have a tendency to develop dissecting aneurysm

Dissecting aneurysm may mimic almost any acute vascular disorder and its masquerades range from the quiet uncertainty which may follow catastrophic syncope leading to shock on the one hand to the urgent agonies of chest pain on the other Baer has divided the clinical masquerades into five different categories (1) The first, the cardiovascular is most likely to resemble acute myocardial infarction with pain, dyspnea, fever, leucocytosis, friction rub, and perhaps congestive failure If the coronary mouths are dissected, actual infarction may occur The other cardiovascular variety resembles thrombosis or embolus of a large vessel (2) The neurological is perhaps the commonest masquerade to be mistaken for an orthodox stroke or apoplexy as may occur with a neurological masquerade of acute myocardial

infarction.* Hemiplegia, peculiar mental or emotional behavior, slowly or rapidly progressing to shock or coma may appear without any previous history of pain or distress. Infarctions of segments of the spinal cord from pinched off intercostal or spinal arteries, monoplegias, paraplegias, hemiplegias, all may occur. The experienced neurologist has learned to be on the lookout for dissecting aneurysm in such clinical states. (3) This group consists of pulmonary disorders in which hemothorax, chiefly on the left, is mistaken for pleural effusion. Here thoracentesis may be the final fatal blow. (4) Abdominal dissection may be mistaken for primary disturbances of the alimentary canal and there may be erosion of esophagus, stomach, duodenum, bleeding, severe pain in the abdomen, suggesting perforation of a peptic ulcer, pancreatic or mesenteric thrombosis. Occasionally a mass may be felt which is misinterpreted as suggesting a malignant tumor. (5) The last masquerade is that of renal disease. Logue and Sikes have emphasized pulsation of the sternoclavicular joint as a helpful diagnostic sign. Extensive studies by Wood and his coworkers 25 years ago and Lodwick in 1953 demonstrated the importance of sudden increase in the size of the supracardiac shadow or the remarkable increase in thickness of the aortic wall as reliable signs to which Golden and Weems have added the elegant contrast of angiography. Treatment, which has been symptomatic, should emphasize the avoidance of anticoagulants and the employment of emergency surgical intervention in the hope that the dissection can be removed, repaired, or wired.

PULMONOCARDIAC FAILURE

Kyphoscoliosis may be a disease *sui generis* as in "idiopathic" kyphoscoliosis. Commonly it follows in the wake of paralytic poliomyelitis. When tuberculosis of the spine was the usual cause, longstanding cases with late sequels were rare, but now many persons with such deformities may live for a long time. More than a hundred years ago, however, Peter M. Latham called attention to this disorder in a description which has hardly been surpassed.

"Strange things happen to the heart when the chest is deformed. Its sounds and impulses and resonance be they what they may are now worth nothing at all as guides to diagnosis. The heart is dragged from its proper seat and imprisoned in some strange place and perhaps turned almost topsy turvy by the encroachment of the vertebral column and the approximation of the ribs. And thus cramped in and hooped about with bone at every movement it gives a jar that may be felt and a sound that may be heard in every part of the chest. And this sound which is thus conveyed at a distance is seldom the natural sound, but a loud whiz, the same in kind and loudest in degree which belongs to mechanical impediment from valvular disease. And mechanical impediment there is, but valvular disease there is none. The encroachment cannot be without mechanical impediment and this impediment cannot be without hurt and hindrance first to the functions and then to the structure of such organs as the heart and lungs."

In spite of this clear description the disorder was badly neglected until the classical studies of Chapman, Dill and Graybiel outlined the main clinical features of the disease and recorded much of the previous literature. Victims of thoracic deformities, especially where right sided dorsal kyphoscoliosis occurs, are generally short of breath during the early stages of pulmonocardiac failure. As time goes on, fainting attacks, aggravation of dyspnea upon mild exertion, and palpitation appear. Ultimately cyanosis, peripheral edema, and the classical features of chronic cor pulmonale develop. Initially at least the failure is that of the respiratory mechanism, resulting partly from the mechanical disadvantage of the deformity, partly from the twists, turns and contortions of the air passages, and the similar angulation and buckling of the large and small blood vessels. Added to this there may be actual compression of windpipe, great vessels or the heart itself. Later sometimes adhesions add an impediment to the

heart's diastolic relaxation or the proper excursion of the lungs. Vital capacity declines as does maximal breathing capacity. The work of respiration increases but the proportion of oxygen extracted from the air diminishes. It is possible that there is some analogy between the fainting episodes and cough syncope but this has not been demonstrated. Victims of this disorder are likely to be plagued by chronic pulmonary infections which of course add to the disability. Where there is muscular paralysis this adds its impediment. Atelectasis, infection and fibrosis may all come into the picture. Since the architectural changes in one who is a hunchback develop slowly, a surprising degree of accommodation may occur in heart and great vessels as well as the tissue of the lung itself but ordinarily the lungs retreat to provide room for the encroachment of the larger vascular structures and the heart itself.

After dyspnea and tachycardia have persisted for a time, cough, faints, cyanosis and edema develop. Intolerance to morphine is common. Some patients with chronic arterial unsaturation tolerate a surprisingly high CO level which is not as important in regulating respiration as the concentration of oxygen, a situation well known in certain forms of emphysema. After death one finds the structural deformity and lesions related to it, a considerable degree of enlargement of the right ventricle and a tendency for hypoplasia, mechanical distortions and infection of the lungs. It is possible that reduced ventilation in the lungs itself may lead to local constriction of the pulmonary arterioles and precapillaries which give rise to increased pulmonary arterial resistance. Actual studies in a few cases have demonstrated increased pulmonary vascular pressure. To what extent other factors are important in the pathogenesis of this condition research has not indicated.

TREATMENT

Once cardiopulmonary failure is established treatment is singularly ineffectual. One's main objective therefore should be to prevent the physical deformities of the chest in which kyphoscoliotic heart disease may be expected to occur. Various methods of correcting such complex lesions have not been very effective up to the present time. The employment of diuretics, cardiac stimulants and oxygen have not been particularly helpful in treating patients with cardiopulmonary failure though there is very little else that can be recommended except orthodox therapy for congestive failure.

HEART FAILURE IN THE GROSSLY OBESE

Though Dickens' fat boy in *Pickwick Papers* is the modern prototype of extravagant obesity, the lay and medical writings of all lands and of all times and places indicate that the social and medical risks of corpulence are well known. In addition to the pathetic or ridiculous aspect there is another problem which has received detailed attention and quantitative study only very recently. This is congestive heart failure in extremely fat persons, reversible with loss of weight. During the past 10 years we have had under observation three enormously obese persons, so fat they had to be weighed with each foot on a separate scale and large scales at that. Two beds lashed together or a specially constructed chair were required to accomodate them. These patients had as a sequel to their vast obesity congestive heart failure manifested by dyspnea at rest, pain in the chest, cyanosis and edema crowding on the fat, indicating that clinically at least water and oil may mix. These patients were enormous feeders and came from families large in size and large of appetite. Their obesity was the primary cause of heart failure as indicated by the relief of symptoms of heart failure during a prolonged course of rigid calorie restriction. In one of the patients the return of failure led to death when she returned to her gluttonous habits. At autopsy no lesion other than considerable fatty deposit in and around the heart muscle could be found to account for her difficulty.

The mechanism by which cardiac failure

occurs in extremely obese people are variable and no doubt in different persons different factors may predominate. It is taught traditionally that each extra pound of fat harbored by an adult adds a requirement for circulation through an additional 20 or so miles of capillary blood vessels. This figure no doubt is inexact, but it indicates one of the circulatory loads. Physical effort in terms of foot pounds must go up and this in turn is reflected in the strain on the heart. Perhaps fat in and around heart muscle produces some mechanical impediment but we have no exact way to measure this. Persons who have "fatty degeneration" of the heart at autopsy may have had little or no sign or symptom of circulatory difficulty. One of the main causes of trouble is the encroachment of the contents of the vast and corpulent abdomen upon the thoracic organs, cramping the quarters of the heart and lungs. This produces some of the same kind of difficulty which occurs in cardiac failure with kyphoscoliosis. The excursion of the chest is impeded, vital capacity and maximal breathing capacity are lowered, oxygen saturation declines and ultimately impaired renal function, sodium and water retention and the entire train of clinical manifestations of congestive failure develop.

Treatment consists of rigid, compulsive and continued restriction of calories until natural body weight is reached. Then hold the line! Some improvement may occur with salt restriction since this ordinarily gets rid of at least some of the edema and thus eases the patient's symptoms. Dietary restriction at best is a difficult process especially in persons who have preferred the social ostracism of fatness carried to the degree of caricature to the restraints and moderation needed for normal existence.

ARTERIOVENOUS FISTULA

Arteriovenous fistulas of clinically important size may occur at any location in the body with adjacent artery and vein of appropriate size. One form may occur after trauma. Healing of a wound which has disrupted vein and artery simultaneously may occur with a direct connection between the artery and vein. This expands and gives rise to a anastomatic vascular tangle growing as time goes on. Cirsoid aneurysms occur in association with such dysplastic conditions as the Klippel-Trenaunay syndrome with considerable deformity of a limb beneath a large nevus and the Sturge-Weber syndrome with an angioma in the distribution of the trigeminal nerve and a similar aneurysmal change in the brain underlying it. Pulmonary arteriovenous fistula is very commonly an accompaniment of Osler's disease (hereditary hemorrhagic telangiectasia) though it is not certain that all cases actually fall into this classification. The strain which a sizable pulmonary A-V aneurysm puts on the body is that of anoxia for a substantial portion of the blood gets through the lungs without being aerated. Peripheral arterial venous aneurysms in the much higher pressure systemic arterial system overload the circulation by providing such a free runoff of blood that cardiac output must be increased to keep the blood flow adequate. The adjustment includes speeding the pulse and increasing the stroke volume. The dynamic situation of fast runoff produces a high pulse pressure and the clinical signs such as Duroziez's murmurs, pistol-shot sounds, capillary pulsation and a tendency to have a warm, moist skin. The blood volume increases, the venous pressure rises. The vascular structure of the aneurysm itself undergoes changes in keeping with the altered pressure within the aneurysm itself. Edema of a limb distal to A-V aneurysm may occur without other signs suggesting congestive failure. After a time the heart may enlarge and in situations where treatment is refused or technically impossible, high output failure may occur. If a large shunt is abruptly but temporarily obliterated by pressure there is an almost instantaneous decline in pulse rate of around 20 beats per minute (Branham's sign), a slight elevation in arterial pressure and a slight fall in cardiac output and venous pressure. In many instances modern-day

surgery is able to produce a complete cure by reconstituting the normal vascular pathways with excision of the aneurysmal sac or by obliterating it As a rule cirsoid aneurysms and the congenital anomalies of skin and underlying tissues are much harder to cure or control by operation

HEART TUMORS PRIMARY AND METASTATIC

MYXOMA OF THE LEFT ATRIUM

The classic example of tumor of the heart is myxoma of the left atrium which may make itself known by manifestations of congestive *failure peripheral gangrene and curious syn*copal attacks in which the orthostatic position is intolerable but the recumbent position is associated with quick improvement particularly if the patient has fallen in a faint The clinical signs are most often mistaken for those of mitral stenosis though the history of rheumatic fever is usually negative The commonest clinical error is mitral stenosis for which an operation may be recommended There are cases on record of operations undertaken with a confident diagnosis of mitral stenosis, the valve being found perfectly normal at operation and a myxoma either being *found and removed or found and left* Rarely the myomatous tissue has been so much like jelly that the gloved finger failed to detect it *and the mystery was resolved only post mor*tem Since technically operations for dealing with a tight mitral valve or a partially occluding myxoma present widely different problems, preoperative diagnosis is not only desirable but essential The primary tumor is usually pedunculated and often arises in the left auricle in the region of the fossa ovalis Trouble comes only when the tumor is large enough to interfere with filling of the auricle or when it encroaches upon and sometimes intermittently occludes the mitral opening There has been some argument as to whether these tumors represent a peculiar kind of organization and degeneration of old thrombotic material or whether they are indeed benign neoplasms The concensus favors neoplastic origin Escaping fragments may produce systemic arterial emboli, and if a large one goes to one of the limbs its removal with identification of the embolic material may permit a correct diagnosis of the heart lesion Not only do the clinical features suggest mitral stenosis but right ventricular hypertrophy and organic vascular change in the pulmonary vessels may occur Features which should help in suspecting a correct diagnosis include (1) The lack of history of rheumatic fever, (2) occasional peripheral emboli with material which may be identified, (3) the paradoxical onset of dyspnea and cyanosis with change in position *particularly with the assumption of the upright* position (4) progressive intractable heart failure, (5) occasional pain and palpitation *with arrhythmias, (6) rarely significant altera*tion of murmurs with change in the position of the body presumably with movement of the pedunculated intra atrial tumor, *(7)* syncopal attacks in which recovery may occur when the patient falls to the floor as though the cork had been burst out of the mitral valve, (8) specific findings of an intra auricular mass detected by angiography, (9) discovery at operation, (10) intractable congestive failure which does not respond to treatment as one would expect in rheumatic lesions of the mitral valve (11) relentless progress of the disorder, (12) symmetrical peripheral gangrene Less common are paradoxical orthopnea with the patient preferring to lie flat x ray evidence of an enlarged left auricle, Adams Stoke's attacks and sudden death Electrocardiographic evidence is non specific but may indicate right ventricular preponderance High sedimentation rate is common and thus may confuse the issue with active rheumatic fever Myxoma should be considered in all cases where mitral *stenosis is suspected of being the lesion but the* clinical course of the patient is bizarre or response to therapy atypical The treatment by surgical removal has led to cure *If the lesion* is recognized first at operation, probably it should not be removed unless cold anesthesia

or an extracorporeal pump are available to permit the surgeon to operate in a relatively bloodless field

BALL VALVE THROMBUS

Ball valve thrombus may present the train of clinical features which are not to be distinguished from those of myxoma Almost always the thrombus occurs in a dilated left auricle in association with definite and frequently tight mitral stenosis The surgical correction of mitral stenosis may be hampered by a ball valve thrombus which should be removed with the usual precautions against embolism

OTHER TUMORS

The heart may be the site of primary neoplasms benign or malignant and metastatic tumors which arrive by way of the blood stream or which invade the heart directly from contiguous structures In addition to myxoma of the left auricle there are other primary tumors of the heart but it is by far the most common The signs and symptoms and the havoc produced depend upon the portion of the heart affected the extent of the disorganization of structure and deterioration of function and if it is metastatic the extent and variety of the primary tumor and other metastases In an aging population tumors in and of the heart have become frequent enough so that their diagnosis no longer smacks of clinical virtuosity Clinical features of tumors of the heart are so erratic as to defy generalizations If congestive failure occurs it is likely to be intractable and fail to respond to the usual measures just as is true of most forms of primary heart muscle disease leading to heart failure Arrhythmias pain bloody pericardial effusion strange x ray shadows electrocardiographic changes of almost any variety atypical and bizarre clinical behavior should lead to the suspicion of neoplasm Cancer of the lung and tumors invading the pericardium from adjacent structures constitute the large bulk of metastatic tumors In some instances a tumor growing in the sluggish streams of the inferior vena cava may get up into the right auricle and in fact may interfere with the proper closure of the tricuspid valve and thus produce a mechanical impediment of an unusual variety Metastatic tumors of hypernephroma may behave in this unorthodox fashion Implants of metastatic neoplasm in the endocardium rarely produce any specific signs and symptoms The common primary tumors are myxoma rhabdomyoma and various forms of sarcomas Hemangioendotheliosarcomas are found occasionally Angiography may be helpful X ray may reveal stubbornly progressive enlargement of the cardiac shadow Both primary and secondary tumors of the heart will probably continue to present baffling clinical problems even though they are increasingly frequent With large numbers of persons dying of cancer these days cardiac involvement in many of them means that a great many people have cardiac metastases More accurate and detailed studies suggest that actual involvement of the heart is found in as many as 20% of persons with primary carcinoma elsewhere[67] Not only do the ordinary carcinomas and sarcomas have this risk but persons with melanomas leukemias and lymphomas may have cardiac metastases adding their weird symptoms and signs to clinical problems already vexing enough

INFECTIONS AND RELATED DISORDERS OF THE HEART

TUBERCULOSIS OF THE MYOCARDIUM

Since tuberculosis has become less frequent as a chronic debilitating disease tuberculosis of the myocardium might be supposed to be dying out but there are indications that it may in fact be increasing It has been encountered chiefly in far advanced disseminated tuberculosis though occasionally generalized tuberculosis may not have been diagnosed previously Sometimes no other active focus of tuberculosis may exist in a person found to have tuberculosis of the myocardium The in

fection gets to the heart through the blood stream, lymphatics, or by direct extension from the pericardium. It may lead to calcification which needs to be distinguished from pericardial calcification or calcific changes within the valves or valve rings. Where the disease is recognized during life, the clinical features are those of tuberculosis with added elements of the heart failure. Rarely there may be rupture into the pericardium.

Treatment should be directed at the underlying tuberculosis by the usual measures of chemotherapy, rest, and a direct attack of extracardiac lesions which may need to be removed surgically. Congestive failure refractory to the proper use of orthodox treatment suggests the possibility of tuberculosis of the heart in a person who has tuberculosis, though other forms of heart failure are more common.

THE HEART IN POLIOMYELITIS

A number of viral diseases may give rise to myocarditis. In some cases of myocarditis a viral etiology is assumed though it may never have been demonstrated. In acute anterior poliomyelitis, the heart may be affected by a true myocarditis, or there may be merely temporary arrhythmias, or the heart may be entirely normal clinically or at autopsy. As a general rule, the degree of involvement of the heart is likely to run parallel to the severity of the infection. Fulminating bulbar poliomyelitis may damage the heart by irritation of the autonomic ganglia and nerves. Myocarditis has been found at autopsy in somewhat more than half the autopsied cases of poliomyelitis. The clinical features of any affection of the heart may be lost in the more dramatic and overpowering bulbar signs in which respiratory failure plays the predominant role. Hypertension may occur and pulmonary edema may develop in some instances with a sound myocardium presumably because of irritation via autonomic nerves from the diseased medulla. In other cases, the left ventricle may be diseased and muscle weakness from the inflammatory reaction leads to heart failure. In bulbar poliomyelitis there may be generalized cardiovascular collapse which probably has both central and peripheral sources. It is likely to occur early in the course of the disease and will be influenced unfavorably by the advent of respiratory failure, tachycardia, shock, and all of the tremendous emotional disorders which this terrifying disease produces in its publicity-sensitized victims. Treatment of the condition depends largely on the general management of the patient rather than a specific therapy directed at the heart itself, which responds rather poorly to the usual cardiotonic and sustaining measures.

MYOCARDIAL TRICHINOSIS

Heart muscle may supply a nidus for trichinae, and if the infestation is extensive cardiac lesions may cause fatal arrhythmias or, rarely, congestive failure. The diagnosis may be easy if we recognize the significance of sore muscles, eosinophilia, inflammation of the conjunctiva most intense near where the rectus muscles are attached, and a history of eating raw pork which may masquerade in hamburgers and other meat mixtures. Eosinophilia may not occur in fulminating infections. The sedimentation rate is not accelerated. Electrocardiographic changes are common, nonspecific, and do not necessarily indicate a bad prognosis. Death may occur from the overwhelming force of the trichinosis with a "toxic" clinical state suggesting that destruction of large masses of muscle may literally intoxicate the body. Some of the cardiac manifestations may result from such processes rather than the invasion of the myocardium. In severe cases, the use of cortisone or other steroid hormones as emergency treatment has been followed by recovery when the outcome had seemed hopeless. If the disease is mild, supportive treatment is ample. No value has been reported from ordinary measures for heart failure such as use of digitalis, low salt programs or oxygen.

ECHINOCOCCUS DISEASE OF THE HEART

Of those diseases which are outrageously obscure, perhaps the most striking is hydatid disease of the heart. Infestation with echino

coccus is for us in the United States a rare disease and it is a fabulously rare disease when it involves the heart This Paul Bunyan among cardiological rarities has been discussed by Canabal Aguirre Dighiero Purcallas Baldomir and Suzacq who have reported no less than three patients with echinococcus disease of the left ventricle diagnosed operated upon and to all appearances cured Since it may remain latent for some time and only reveal its presence when a myocardial cyst ruptures into a chamber of the heart or into the pericardium it is important to diagnose it early Fluoroscopic and roentgenologic studies may reveal a localized deformity in the outline of the ventricle sometimes with elegant marginal calcification Occasionally spotty or irregular calcifications may outline the wall If the lesion is strategically located angiocardiography may reveal a filling defect within the ventricular cavity Electrocardiographic changes are consistent with what one would anticipate in a localized lesion which disrupts the continuity of active ventricular muscle or active myocardium Since the cardiac aspects of this disease are potentially curable by surgical removal of the cyst early diagnosis is important but is not apt to be made except where the disease is common enough to be considered in differential diagnosis

SARCOIDOSIS

Among the subtle causes for sudden death unrecognized sarcoidosis is encountered from time to time In this disorder we find various arrhythmias syncopal attacks Stokes Adams seizures with or without an ultimate end in sudden death In addition to the arrhythmias the electrocardiographic abnormalities—bizarre various and nonspecific and their clinical counterparts in palpitations and throbbings congestive heart failure may occur Usually it is rapid in onset fulminating in course and soon leads to death The carotid sinus may or may not be sensitive Anginal pain occasionally may be a feature of the disorder The pulmonary lesions of sarcoidosis with diffuse granulomas and fibrosis or extensive pulmonary lymphadenopathy may impede the flow of blood through the lung and lead to cor pulmonale

Since the cause of sarcoidosis is not clearly understood specific therapy is not available and treatment of the heart trouble itself being symptomatic is generally unsatisfactory When the lesions in the myocardium interfere with cardiac function pure heart muscle failure may result It is relatively refractory to treatment Though the very nature of sarcoidosis is not known tuberculosis usually stalks near by

KARTAGENER S SYNDROME

As happens so often with eponyms the name of Kartagener is attached to a syndrome which he popularized but which had been described by someone else in this case three decades earlier by Stewart Dextrocardia usually with transposition of the viscera often has a curious sequel in the common occurrence of bronchiectasis There may be aplasia or absence of the frontal sinuses with infection of the ethmoid and maxillary sinuses It is not known whether dysplasia or deformity of the bronchial system favors the development of bronchiectasis Studies from nose and throat specialists rarely include examination of the heart so figures of incidence begin with dextrocardia or bronchiectasis The treatment of bronchiectasis in Kartagener s syndrome is neither different from nor better than that for ordinary forms of bronchiectasis

OBLITERATING ENDOCARDIAL SCLEROSIS

FIBROELASTOSIS OF THE ADULT

The endocardium of the heart may become replaced by a fibroplastic sclerosing lining which ultimately produces a dynamic effect indistinguishable from that of a similar constricting restraining pericardium Whether this condition should be considered an allergic reaction merging into the kind of case with

extreme eosinophilia which was first described by Loeffler in 1936 or whether this should be properly considered one of the cardiovascular collagenoses with parietal endocardial thrombosis the sclerosis being the ultimate stage in the healing an earlier stage being the deposit of fibrin on the endocardium, or indeed whether it is a separate disorder related to the fibroelastosis of infants a possible congenital anomaly cannot be settled with present information In adults the course may resemble that of a completely mysterious heart muscle failure The dynamics are those of constrictive pericarditis The therapy for ordinary heart failure is singularly and regularly ineffectual Occasionally the symptom complex of angina pectoris prevails presumably because of ischemic changes though the symptoms are proportional to the involvement of endocardium and heart muscle rather than the state of the coronary arteries which may be healthy There are no really satisfactory ideas about this condition and no helpful methods of treatment We do not even understand what kind of a disease it is Is it dysplastic congenital related to some distorted hypersensitivity mechanism a peculiar scarring produced from fibrin deposits on the endocardium a collagen disease or something else? It may in fact turn out on further study to be a composite rather than a single disease

LOEFFLER S SYNDROME

Loeffler s syndrome of the heart is placed in that vaguely bound realm of rare diseases where reside conditions characterized by the unusual deposits of collagen The presumed sensitivity disorders such as polyarteritis nodosa and certain conditions such as Loeffler s syndrome with transitory infiltration of the lung and eosinophilia are as obscure in origin as they are difficult in treatment In some instances the pulmonary infiltration has been severe enough to put some load on the right heart though this rarely reaches the point of clinical significance This disorder is reversible though by what means Nature produces improvement and cure we do not know Opportunities for extensive study of pathological material have not presented themselves Thus there are occasional patients who have eosinophilia pulmonary infiltrates and usually transitory cardiac irregularities and electrocardiographic changes rarely congestive failure in whom some benign disorder of the heart accounts for the relatively minor signs and symptoms Treatment rarely necessary is of little or no value

AMYLOIDOSIS

Primary cardiac amyloidosis is a rare disease which generally affects middle aged or elderly persons The mechanical impediment produced by the infiltration of amyloid into the interstices of the myocardium gives rise to the clinical state of pure heart muscle failure About the only clue to diagnosis is the exclusion of other possible entities though occasionally an enlarged tongue may be helpful In primary amyloidosis the Congo red test offers very little assistance in making the diagnosis In 1948 Findley and Adams noted striking similarities between amyloidosis of the myocardium and pericardial constriction the essential feature being the difficulty of diastolic filling of the ventricle which may be recorded as a high end diastolic pressure These observations have been verified and extended by Gunnar Dillon Wallyn and Elisberg Couter and Reichert Since physically contraction of the heart is impeded by the infiltration of amyloid the circulation labors under the unusual handicap of high diastolic filling pressure and relatively low systolic pressure Use of cardiac catheterization and other refinements in diagnosis may make it possible to suspect the disease where it is not clearly suggested on clinical grounds Amyloidosis is an important sequel in about a quarter of the patients who die from multiple myeloma In such circumstances involvement of the heart is commoner than in the other diseases associated with secondary amyloidosis so that one needs to consider amyloidosis in anyone with multiple mye

loma who develops congestive failure In other forms of secondary amyloidosis however invasion of the heart is relatively rare Benford has reported infiltration of coronary arteries with amyloid which may add a further element of disease to the heart Additional emphasis should be placed on the fact that cardiac amyloidosis is a disease which occurs in the years of advanced old age being most frequent after the age of 70

The nature of amyloidosis its relationship to derangements of protein metabolism and the reasons for the bizarre and erratic selection of organs and tissues for amyloid deposit are hidden in obscurity

The usual forms of treatment of the congestive heart failure in amyloidosis are predictably ineffectual and rarely can the primary disease be repaired so that the process resolves

HEMOCHROMATOSIS

Perhaps because therapy with insulin has kept more patients with hemochromatosis alive for long periods late features of the disease have had time to become more prevalent and better recognized In hemochromatosis heart failure may be a cause of symptoms and a cause of death There is much discussion concerning the nature of the heart trouble in hemochromatosis A number of French authors have described a syndrome "endocrino hepato-cardiaque" of a peculiar variety with suggestions of adrenal cortical inadequacy as a fairly common feature of hemochromatosis A number of different forms of endocrinopathy have been reported in individual cases but they could not regularly be explained by obvious disease caused by hemochromatosis in the defective organ The heart failure in hemochromatosis generally occurs late in the disease and in older persons although French authors report their syndrome in younger patients Heart failure may develop insidiously or it may be brisk at onset and fulminating in its progress Occasionally hypoglycemia or diabetic coma may precipitate heart failure A great variety of arrhythmias has been described and likewise numerous forms of electrocardiographic aberration have indicated diffuse but not specific disease of the heart muscle Therapy as in most diseases of the heart muscle itself has been singularly futile In fact there have been suggestions that digitalis may damage the heart rather than help it In contrast to the reports from French authors who do not find much pigment or much direct damage to the heart in hemochromatosis American physicians have found extensive pigment deposits diffuse myocardial fibrosis atrophy vacuolizations and fatty degeneration which together or in varying combinations give ample pathophysiologic grounds to explain the heart failure

DISEASES OF MUSCLE

PROGRESSIVE MUSCULAR DYSTROPHY

It is not surprising that in generalized muscle diseases the heart muscle may ultimately become affected though as a rule in such conditions cardiac muscle and smooth muscle are relatively resistant to the destructive forces giving rise to the disease One of the reasons why disorders of the myocardium were not recognized earlier is that most people with severe muscle diseases are unable to exercise to the point where even the early manifestations of heart failure become manifest Many victims die young Progressive muscular dystrophy is one of a group of myopathies of unknown etiology which occurs in families It is characterized by wasting and atrophy of the striate muscles inexorably advancing weakness and ultimately death Even when one is on the lookout for it its beginnings may be so insidious that a particular time of onset cannot be detected or recalled Usually signs begin during adolescence The

replacement of the atrophic and fibrotic muscle by fibrous tissue and fat may cause pseudohypertrophy. Cardiac lesions caused by the same dystrophic process are now recognized to be fairly common. In very rare instances heart failure of unknown cause may be the presenting finding before the myopathy is recognized. At autopsy the heart is enlarged, hypertrophied and dilated, both ventricles being about equally affected. Lesions in the myocardium include a spotty fibrosis more or less everywhere throughout the heart muscle with areas of acute degeneration and a considerable infiltration with fat. Electrocardiographic abnormalities included changes in the T waves, short P R intervals with a QRS of normal duration, tall R waves in V 1 and 2 and certain other nonspecific Q and T wave changes. They have been found in about three fourths of the cases where such studies were made even in the absence of any signs indicative of heart failure or heart trouble.

The clinical features of dystrophic heart disease are those of heart muscle failure with breathlessness, tachycardia, arrhythmias, ultimately progressing to cardiac enlargement and the signs of congestive failure with nonspecific electrocardiographic changes. Treatment is discouragingly ineffectual.

MYOTONIA ATROPHICA

The heart in myotonia atrophica has been described in detail by Rinsler and somewhat more recently by Spillane. Disorders referable to the heart are likely to occur late rather than early in the disease. Various electrocardiographic changes which are altogether nonspecific have been described. Complexes of low voltage are common as is bradycardia. The blood pressure tends to be low. The heart tends to be small, at least early in the disease. *The first heart sound in the mitral area is likely* to be split. Thus a small pulse, relatively low blood pressure and splitting of the first heart sound in the mitral area are the usual clinical findings and the electrocardiogram may show in addition to bradycardia, low P waves and prolongation of the P R interval. Intractable heart failure may be a late sequel though many persons die of the disease without cardiac symptoms.

PARCHMENT HEART

Segall has called attention to Osler's description of a parchment heart whose walls were so thin in many places as to resemble the tenuous translucency of "sheep skin." Good coronary arteries excluded mechanical impediment to blood supply as a cause. The dilated sac of a heart seemed to have forgotten to hypertrophy. No clinical details are at hand to tell us how the owner of the heart managed to live with such a flimsy bag of waters for a cardiac pump. Perhaps it represents the end point of a generalized muscular atrophy.

ACROMEGALY

Shortly after the early descriptions of acromegaly as a clinical phenomenon heart failure was recognized as a fairly common complication. The mechanisms by which the heart gets into trouble in acromegaly seem to be fairly straight forward. First there is an increased metabolism as well as an increased bulk of the body requiring the heart to do more work. The heart dilates and may undergo massive hypertrophy, sometimes weighing more than 1 000 gm. There is a conspicuous hypertrophy of individual fibers and sometimes rather generalized scarring and fibrosis throughout the myocardium. The intercurrence of hypertension and an occasional disorder of carbohydrate metabolism may add elements of extra strain. The clinical features are those of heart muscle failure. The electrocardiographic changes which are very common are in no way specific and merely indicate myocardial disease. Unless treatment directed at the underlying problem is effective the ordinary measures for treating congestive failure are disappointing.

PULSELESS DISEASE

The syndrome of pulseless disease, which has been called Takayasu's disease, is a proliferating stenosing arterial disorder affecting chiefly the upper part of the body with a situation analogous to a reversed coarctation It is much more common in women than in men and tends to occur in the relatively early years in life up to and including the fourth decade The main disorder is arterial narrowing which may go on to a complete occlusion of the large arteries coming off the arch of the aorta The descending aorta as well as other vessels going to vital organs are not implicated Clinically, the peripheral pulses in the upper extremities and in the neck may be missing The symptoms may be those of cerebral ischemia, petit mal attacks severe convulsions, paralyses and eventually wasting of the muscles of the shoulder girdles, the arms, the neck and of the entire face Characteristic arteriovenous aneurysms in the retina have been described Cataracts are relatively common, presumably resulting from anoxia The lesion is an inflammatory giant cell arteritis with considerable round cell infiltration, together with endomural thrombosis which probably results from the arteritis itself The disease may progress over a period of many years ultimately causing death by cerebral ischemia with either an increasing train of minor difficulties or massive neurologic disorganization

There is no treatment but perhaps the ingrafting of new arterial tubes might be feasible in some cases

SYMMETRICAL PERIPHERAL GANGRENE

In an active consulting practice in medicine, one may encounter patients who have developed symmetrical gangrene of fingers, toes, and occasionally the tips or lobes of the ears, and even the tip of the nose Most such patients have diseases which, interfering with the hearts' activity, give rise to shock and asphyxia of distal tissues, or situations in which a vasospastic element may precipitate a Raynaud's phenomenon Omitting disease of the arterial system itself, such as thromboses from atherosclerosis, embolism, dissecting aneurysm, rheumatic arteritis or thromboangiitis obliterans, there remain several well recognized conditions in which symmetrical peripheral gangrene may develop The most important are those which diminish the cardiac output Of these ball valve thrombus with occasional total though brief obstruction of blood flow, myocardial infarction, acute and severe congestive heart failure, tight mitral stenosis bacterial endocarditis, and paroxysmal tachycardias constitute the largest group Certain infections attended by shock and indeed fever of unexplained origin may be the background mechanism in other examples Meningococcal infection, pneumonia, diphtheria, cholera, tuberculosis and syphilis have been implicated Similar situations where the arteries are occluded occur in thrombophlebitis Disorders of the blood itself including the cryoglobulinemias, autohemoagglutination, and perhaps hemoglobinuria can be mentioned Finally there is a miscellaneous group in which the same lesions may occur in what has started as pellagra or acrodynia, in starvation and in ergot poisoning The important point is that in most instances some underlying process or mechanism can be discovered, sometimes it can be treated, rarely it can be cured There are a few examples where symmetrical peripheral gangrene appears to be a self limited disorder probably a true Raynaud's phenomenon, which begins acutely and progresses to the point of actual gangrene If the underlying condition is recognized and can be remedied, prognosis can be surprisingly good though in many instances it is nothing more than an omen of impending death In this regard it has very much the same significance as the livedo reticularis like state of the skin which often appears in the pre mortal stage of an illness It is rare for persons who display it to recover

Thus, symmetrical peripheral gangrene is a sign which may be produced by a great many different conditions, all of which indicate some difficulty in the peripheral circulation and all of which may have an ominous significance

IDIOPATHIC CARDIOMEGALY

Idiopathic cardiomegaly is a good example of how easy it is to hide ignorance under a high sounding name It is also an example of how much easier it is to write of a disease than to find a remedy for it This disorder may or may not run in families, but there are many examples of several members of a family being affected Its discovery should lead a survey of relatives for latent cases Cardiac failure with cardiomegaly of obscure variety seems to have been described first by Josserand and Gallavardin in 1902 Since that time there have been a number of case reports Several different series having been reported by Levy and his colleagues who have clarified the natural history It is more common in men than in women and perhaps more common in negroes than in whites Usually it occurs under the age of forty It may be asymptomatic for a long time, but after symptoms occur death is usually less than 2 years away Pulmonary embolism is common and systematic thrombo embolism occurs Most patients have congestive heart failure and a few have died suddenly The electrocardiographic changes are common but in no way specific Cause of hypertrophy is obscure Diagnosis is made by exclusion, a thoroughly unsatisfactory situation

Persons who have cardiac enlargement of undetermined cause may be found in x ray surveys and their prognosis is much better than in patients who present themselves with heart failure

At autopsy there is remarkable hypertrophy, the heart s weight in some series averaging between 600 and 700 gm and often reaching 1,000 gm Focal necrosis, degeneration of muscle scattered fibrosis most extensive under the endocardium and mural thrombosis in the absence of significant valve or artery disease, or hypertension, constitute the findings Some have suggested anoxia as a cause but there is no good evidence to support this idea Demuth and Landing have found evidence of widespread hypertrophy of the media of various arteries in the body along with focal endomyocardial fibrosis in some patients with idiopathic cardiac hypertrophy and believe that there may be a connection here with endocardial sclerosis though this is by no means certain The treatment has been uniformly discouraging The heart, grown big for reasons we do not know, wears out and congestive failure, unresponsive to our best efforts at therapy, brings down the final curtain

CARDIOVASCULAR SYNDROME OF METASTATIC CARCINOID

In the last few years serotonin has emerged as a fascinating natural humor in the human body with a variety of functions Serotonin liberated by carcinoid tumors metastasizing to the liver causes a disease complex with acquired lesions of the valves on the right side of the heart functional and structural vascular changes in the skin, hypermotile diarrhea "asthma" and ultimately edema, heart failure and death What we now know as serotonin was recognized through its biological properties by Ludwig ninety years ago when he demonstrated that defibrinated blood contained a powerful vasoconstrictor substance not demonstrable in the same blood before coagulation Rapport, Greene and Page, looking for this mysterious vasoconstrictor, identified it in 1948 Erspamer for many years had been studying an elusive vasoconstrictor material he got from extracting portions of the alimentary canal and this substance turned out to be serotonin Recently hematologists have demonstrated that serotonin occurs in abundance in platelets though apparently a supercargo rather than a vital agent It is active in clot retraction though probably not necessary for hemostasis My associates and I have encountered three patients with the vasculocardiac syndrome of metastatic carcinoid and thus have unusual experience with a rare disease The symptoms of this protracted clinical illness may begin with flushing and blushing This is seen as remarkable vasomotor changes consisting of a tricolored flush, in which elements of cyanosis extreme pallor, and a pink salmon colored blush come and go in a way

that "mimics in clinical miniature the fickle phantasmagory of the aurora borealis" Diagnosis is easily established when the full syndrome is presented with the characteristic vasomotor changes bronchoconstriction with spasms shorter and more erratic than in usual asthma and bouts of hypermotile diarrhea presumably caused by serotonin itself Later in the disease angiomas which resemble coarse flecks of hand ground pepper appear in the skin Added to all this there are remarkable lesions which develop on the right side of the heart primarily The earliest lesion seems to be a proliferation of fibroblasts in a very loose matrix on the valve surface Such lesions may be found on the left side of the heart also by the time those on the right side are very much further advanced A sort of gelatinous proliferation occurs most pronounced on portions of the valve directly exposed to the flowing currents of blood Ultimately the proliferating valve edges may fuse together causing stenosis of tricuspid and pulmonic valves Much experimental work on a number of antagonists suggests that some of the complications of hyperserotoninemia may be prevented if sufficient quantities of the antagonists are available more or less continually In most instances the hepatic metastases are so extensive that surgical attack on the metastatic lesion is out of the question Very simple tests for 5 hydroxytryptamine (serotonin) in the urine are available[142] and these should be useful in screening persons who have unusual blushes or hot flashes The clinical picture in the carcinoid syndrome in no way resembles the more stable mottled blushing of the "hypothalmic" hypertensive or epileptic person and should present no diagnostic difficulties Carcinoids which have not metastasized to the liver apparently either do not liberate as much serotonin as those growing in the liver or the capillaries of the liver are able to abstract neutralize or destroy the material so that it does not flood the circulation and thus produce the valvular or vascular damage As a model for studying an acquired form of heart disease it may throw some light on other more common but more obscure conditions such as rheumatic fever The outburst of papers published about this syndrome since its almost simultaneous description in three different clinics indicates the importance of strategic articles and descriptions of cases in calling attention to unusual syndromes This is one rare disease for which the pathogenesis is well worked out The melancholy theme of therapeutic futility still echoes here too

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Introductory Comment

The references listed here are selective rather than complete The physician who wishes to get further information about rare diseases of the heart and cardiovascular system must read current medical writings industriously and must go to the standard text books on heart diseases and standard monographs on rare diseases for further information Reich has written a volume on uncommon heart diseases which is excellent but unfortunately omits a number of interesting diseases I have found the textbooks by Friedberg Wood and White are invaluable aids in writing this chapter but even more helpful have been the current references in journals of internal medicine surgery and cardiology

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CHAPTER 45

The Prevention and Treatment of Congestive Heart Failure

JOHN FRANCIS BRIGGS M D

IN THE prevention and treatment of congestive heart failure we are faced with the following problems First that of determining the type of heart disease that exists and what precipitating factors are present second what if any associated diseases are present and lastly whether or not the patient has been treated for heart failure previously The object of treatment is to decrease the work of the heart and by doing so to increase its efficiency and to remove such edema fluid as is present in the tissues

There is no specific method of preventing heart failure True it is that by virtue of the prophylactic use of penicillin we may decrease the incidence of rheumatic fever and also abort syphilitic infections before the cardiovascular system is involved The prophylactic use of penicillin in chronic valvular heart disease may prevent the development of acute or subacute bacterial endocarditis Patients with mild heart disease may be precipitated into severe congestive heart failure by virtue of extracardiac diseases that affect the cardiovascular system The effect of malnutrition upon the cardiovascular system either malnutrition in the form of obesity or inanition and anemia is very well known Anemia may aggravate or incite the development of angina pectoris Avitaminosis may be a factor in congestive heart failure and many anomalies of the heart and blood vessels can also incite congestive heart failure The endocrine disturbances particularly of the thyroid gland are notorious for their effect upon the cardiovascular system and hypertension also may be the cause of heart failure Infections involving the heart such as myocarditis endocarditis and the like may be the initiating factors in some forms of heart failure Pericarditis may lead to the development of congestive heart failure and various types of acute and chronic right heart strain may be the underlying cause of congestive failure Mechanical displacement of the heart may cause the heart to fail Almost all these factors are treatable or reversible and treatment directed at them may be sufficient to relieve the congestive heart failure The development of a persistent arrhythmia may be the provocative agent that has caused the heart to fail and treatment directed to the arrhythmia will assist in controlling this failure

The treatment of heart failure requires that the patient be given rest both physically and mentally The patient should be put at rest in the position that gives him most comfort It is not necessary that he remain flat in bed and if the patient finds that he is more comfortable sitting in a chair with his feet elevated there is no reason why this position should not be assumed While at rest a commode and not a bedpan is used The patient is to remain at rest at the position best suited to him until compensation is restored to its fullest At this time the patient is started on ambulation These graduated exercises are best prescribed in a specific pattern If the patient has been in bed, he is first allowed to sit up with his feet dangling over the edge of the bed for 20 minutes three times daily for 2 successive days If this causes him no trouble he may then be removed to a chair where he sits for 30 minutes

three times daily for 3 days If no untoward symptoms develop the length of time in the chair is increased by thirty minutes every third day until the patient is up 8 hours a day This is continued until the patient is returned to full activity unless he is restricted by some adverse symptoms that have developed in this process of graduated activity If the patient is able to be up for at least 30 minutes four times a day and the bathroom is in the same room as the patient the patient is then permitted to use the toilet When he is up for 30 minutes four times a day graduated walking exercises can be started The patient commences by walking the equivalent of one half a city block three times a day for 3 days and then increases this every third day until he returns to full physical activity unless he is limited by some symptom that may develop in the process of this graduated activity At the same time the patient is permitted to walk one half flight of stairs three times a day for 3 days and if no symptoms develop he may then be permitted to walk a full flight of stairs three times a day for 3 days At this time if no unfavorable symptoms appear he may continue to walk the stairs as he desires The purpose of the graduated activity is to restore the muscle tone of the patient and more important to inform the physician and the patient to what extent improved cardiac function has returned No limitation must be placed upon the individual by the attending physician except those limitations that are placed upon the individual by his limited cardiac reserve If the cardiac reserve returns to normal or near normal the patient should be returned to as nearly a normal social economic, and community life as is consistent with the return of this function If on the other hand the graduated activities indicate that the patient has a poor cardiac reserve, he is taught to restrict his activities to the limitations that have been placed upon him by his heart

Diet plays an important part in the treatment of congestive heart failure A diet low in the sodium ion is of course essential for the removal of edema fluid A diet containing 400 mg of sodium is easily prepared If the patient is obese the caloric value of the diet is reduced to 1200 calories per day During this time the fluid intake is limited to 2 000 cc per day and the diet is supplemented by one of the multivitamin preparations During this time the patient is weighed daily and the fluid intake and output is measured so that one can determine the progress of the patient The patient remains on the diet and the fluid restriction until maximum effects are obtained The diet may then be altered empirically to suit the needs of the individual In the acute phase the diet may be managed by restricting the patient's total fluid and food intake to 800 to 1000 cc of skim milk daily for one week This often produces excellent results in the control and management of the edema

Drugs are very important in the treatment of congestive heart failure and a great many drugs are used in its treatment Those that will be mentioned in this chapter are those in common usage No attempt will be made to outline all the various digitalis and other cardiac preparations

Acidifying agents may be used in the treatment of congestive heart failure Ammonium chloride given in the dosage of 90 grains daily 4 days a week until maximum diuresis has occurred often proves very valuable At the end of this time the patient may be placed on a maintenance dose of ammonium chloride of 15 grains four times a day 4 days a week to enhance the diuresis and to increase the action of the mercurial diuretics

Aminophylline is seldom used in the oral form but the intravenous use of aminophylline in doses $3^1/_4$ to $7^1/_2$ grains given slowly is an effective method in the treatment of pulmonary edema acute nocturnal dyspnea and other phases of congestive failure One may also use suppositories of aminophylline

The use of anti coagulants is a controversial subject in the treatment of congestive heart failure Should one want to use the anticoagulants and want a rapidly acting one heparin is suggested At the onset of treatment the coagulation time is determined by the Lee-White method and at the same time the prothrombin activity is determined Heparin is then given in a dose of 50 mg in sterile water intravenously every 4 to 6 hours and this is continued so that the coagulation

time remains between 30 and 60 minutes At the start of the heparin therapy 300 mg of dicumarol is given by mouth if the prothrombin time is normal 200 mg is given on the second day and 100 mg is given on the third day The prothrombin activity is determined daily and the coagulation time every 12 hours As soon as the prothrombin activity is between 20 and 30% of normal the heparin treatment is stopped The dicumarol is now used in such dosage as to maintain the prothrombin activity between 20 and 30% of normal Occasionally one may use a depoheparin in doses of 200 to 300 mg intramuscularly This may be repeated as often as necessary to control the patient s coagulation time If there is no urgency to obtain full anti coagulation effect dicumarol may be used alone The anti coagulant therapy is maintained until the patient is up and about Whether or not one should continue prolonged anti coagulant therapy is a controversial question

Cathartics are used in the treatment of congestive heart failure and a lubricant type can be used effectively to keep the bowels loose in order to prevent straining at the stool

Digitalis preparations are many in number The important thing is to select for usage one oral whole leaf product one oral glycoside and one intravenous product Once having made the selection the physician should become thoroughly familiar with their usages and contraindications The whole leaf product to be here described is digitora in which the 1 28 grain tablet is equivalent essentially to one cat unit of digitalis The oral glycoside selected is digitoxin which comes in 0 1 0 15 and 0 2 mg tablets The intravenous preparation selected is cedilanid of which 8 cc when injected intravenously is the average digitalizing dose Occasionally people will have difficulty with digitalis products and some substitute must be used in these instances Squill in the form of the "urginin tablet is used as a substitute for digitora and ouabain in a dose $^{1}/_{120}$ grain intravenously is selected as the intravenous preparation There is only one indication for the use of digitalis except in the treatment of arrhythmias and this is heart failure Digitalis must be given until the full therapeutic effect is obtained and then this digitalizing effect must be maintained by the daily use of an adequate maintenance dose There is no effective scheme by which a patient can be guaranteed to be digitalized but a routine procedure is often effective and practical For this purpose it is suggested the digitalizing dose of the whole leaf product be one cat unit for every 10 pounds of body weight Thus an individual weighing 180 pounds should be digitalized with the oral administration of 18 cat units of the whole leaf We must recognize that some patients will be digitalized before the entire 18 cat units are administered and others may require up to 25 cat units of digitalis before the patient is full digitalized If the patient s condition does not make rapid digitalization urgent one tablet of digitora may be given four times a day for 4 days Since the patient excretes about one cat unit daily he has an effective digitalizing dose of 3 cat units daily so that in the four day period he will have lost four cat units of digitalis and retained a total of 12 cat units He then receives digitora grains 1 28 three times a day for 3 more days He loses approximately 3 cat units during this time in the urine but he has retained 6 cat units giving him the effective dosage of approximately 18 cat units of digitalis At this time the patient should be fully digitalized if not the dose is continued three times a day until full digitalization has occurred When digitalization has occured the dose is cut to a maintenance dose which varies from $^{3}/_{4}$ of a grain to as high as three grains of digitalis daily The maintenance dose must be determined in each individual case For rapid digitalizing the whole leaf product may be used but digitoxin is a more effective method It is absorbed almost in toto and very rapidly from the gastro intestinal tract The average digitalizing dose is from 1 2 to 1 8 mg This may be given in one dose Here again one risks the possibility that in some individuals this is an excessive dose whereas in others it is insufficient If the dose is not sufficient one may continue giving 0 2 mg every half hour until digitalization has occurred If the condition does not warrant single doses of such magnitude the patient may be digitalized by taking 0 2 mg of digi

toxin every half hour until digitalization is complete. Once digitalized the patient is maintained with a daily dose of digitoxin. The maintenance dose varying from 0.1 to 0.2 mg. daily.

If the patient is unable to take oral medication cedilanid may be given intravenously. This may be given in one injection recognizing again that it may be too much digitalis for one individual and too little for another. If the condition is not urgent 4 cc. is given intravenously and 2 cc. every hour until the patient is digitalized. The maintenance dose intravenously varies from 2 to 4 cc. daily. One may switch to any type of digitalis with which digitalization can then be maintained. In doing so use the ordinary maintenance dose of the selected drug but recognize that in doing so the rapid excretion of the drug may result in the loss of digitalization. Should this occur it is suggested to redigitalize using the substitute product.

It is important in the use of digitalis to remember certain facts: (1) never digitalize a patient rapidly if he has been receiving digitalis recently; (2) digitalize the elderly or the aged patient less rapidly; (3) don't digitalize a patient rapidly who has had a recent myocardial infarct; (4) should the patient have been on whole leaf digitalis previously use digitora grains 1 28 three times a day until digitalization has occurred or digitoxin 0.2 mg. may be given every three hours until the desired effect has been produced; (5) do not give the first doses of a mercurial diuretic just at the completion of digitalization as it may precipitate digitalis intoxication; (6) do not give intravenous calcium salts when using digitalis as these may produce undesired arrhythmias; (7) if the patient is not digitalized after an adequate dosage suspect the existence of an associated complicating condition.

Hypertonic glucose may be used in the treatment of congestive heart failure whenever indicated.

Opiates are very important in the treatment of congestive heart failure. Morphine sulphate grains 1/4 with atropine sulphate grains 1/150 is suggested. Should the patient be sensitive to morphine a different opiate may be substituted.

Oxygen may be life saving to the individual with congestive heart failure. It may be administered by mask, by tent or by nasal catheter. Oxygen must be administered carefully if the individual suffers from emphysema or chronic cor pulmonale. The use of 100% oxygen may precipitate respiratory acidosis and apnea. In these instances it is much better to use an oxygen mixture.

Sedative and tranquilizing drugs may also be used. Equanil in a dosage of 400 mg. four times daily or mebaral grains 1/6 four times daily is suggested.

In patients with intractable congestive heart failure it may be advantageous even in the euthyroid patient to make the individual hypothyroid by the use of radioactive iodine. The dosage should be individualized.

There are a great many mercurial diuretics available for the treatment of congestive heart failure. These may be given intravenously, intramuscularly, orally or by rectal suppository. In addition fluid may be removed mechanically by thoracentesis or by paracentesis. In massive peripheral edema Southey tubes may be effective.

Bleeding the patient when venous pressure is very high is also effective in the treatment of congestive failure. The same result may be accomplished occasionally by use of tourniquets around the four extremities and then releasing them progressively and slowly. Salyrgan theophylline is given intramuscularly in a dose of 1 cc. at the beginning of the treatment and it may be repeated every second day until maximum diuresis has occurred and the patient's weight becomes stable. The interval between injections of a diuretic is increased gradually. The length of time between injections varies with each patient but many individuals may go for 1 week or longer before an injection is again needed to keep his edema under control. Many times the continued use of a regular dose of a mercurial diuretic at intervals will not only control the edema but will prevent the development of acute pulmonary edema. This prophylactic use of the mercurial diuretics is important. If the patient is in an area where a physician's services are not obtainable the patient is taught to weigh himself daily and give his

own injection of a mercurial diuretic He follows his routine and on the day that he notices an increase in weight he takes his mercurial diuretic intramuscularly

Acute heart failure is often termed cardiac asthma paroxysmal nocturnal dyspnea or acute pulmonary edema It represents a seizure due to acute left ventricular failure The treatment is always urgent The patient should be given morphine sulphate grains $^{1}/_{6}$ or $^{1}/_{4}$ intravenously This is almost specific in relieving the symptoms If the patient does not respond he would then be given $7^{1}/_{2}$ grains of aminophylline with 1 cc of salyrgan theophylline intravenously slowly Before the injection it may be wise to insert an indwelling catheter for often the rapid diuresis may result in urinary retention If relief has not been obtained the patient should be rapidly digitalized with either digitoxin orally or cedilanid intravenously If all these measures do not bring relief one may bleed the patient and at the same time administer oxygen. In severe cases the patient should be hospitalized Since this condition represents an attack of acute congestive heart failure it will, in all likelihood return The patient should therefore be treated as any individual suffering from chronic congestive heart failure with the use of sodium restricted diets digitalis diuretics etc as indicated

Intractable heart failure occurs at times If the treatment proves ineffective review all of the medications to determine whether or not the patient has received maximum drug therapy One should always consider the possibility of a complicating disease which may be aggravating the congestive heart failure such as hyperthyroidism etc Further one should determine whether or not the underlying cause of the congestive heart failure may be benefited by surgery In intractable heart failure suspect the possibility of a coexisting silent myocardial infarction which may occur without warning and without diagnostic symptomatology

Electrolyte imbalance may also be a factor in the refractory phase of congestive heart failure In one type the sodium level remains normal but the chloride level drops below its normal range When this happens there is an elevation in the bicarbonate of the blood and frequently a diminution in the potassium This is known as hypochloremic alkalosis with or without hypokalemia This may be best treated by giving the patient ammonium chloride and the potassium if it is indicated The second type of electrolyte imbalance is one in which both the sodium and the chloride levels become lowered and an acidosis results This can occur in individuals on a low sodium diet This type of electrolyte imbalance is always difficult to treat because it is associated with a severe degree of heart failure It is treated by giving the patient sodium chloride and by temporarily stopping the use of mercurial diuretics In the severe hyperchloremic acidosis, the patient may be treated by the intravenous use of $^{1}/_{6}$ molar sodium lactate solution Nutritional disturbances such as vitamin B deficiences can occasionally cause intractable failure Many times the control of a persistent rapid arrhythmia may be all that is necessary to stop the intractable heart failure

The time finally comes in the treatment of congestive heart failure when the heart is no longer able to maintain the circulatory demands placed upon it and all treatment fails

An illustration* of the management of a patient with congestive heart failure may be outlined in the following procedure for an obese male 180 pounds in weight

(1) He would be placed in bed a portable commode supplied to him and he would remain in bed until maximum compensation had been established then he would be permitted to be up on graduated exercises

(2) Since he is obese, he would be placed upon a 1 200 calorie low sodium diet Fluids would be restricted to 2 000 cc a day The fluid intake and output would be measured, and a multiple vitamin capsule would be administered Ammonium chloride grains 15 six times daily would be administered for 4 consecutive days then omitted for 3 days and administered again for 4 consecutive days This would be continued until the patient had maximum diuresis and then the patient would be placed upon 15 grains of ammonium chlo

* "The treatment of congestive heart failure" *Minnesota Medicine* 34 Nov 1951

ride three times a day for 4 days out of each week Aminophylline would not be administered unless the patient was having a marked pulmonary edema or seizures of cardiac dyspnea or cardiac asthma In this event the patient would be given $7^1/$ grains of aminophylline intravenously slowly as needed to relieve the symptoms The anticoagulant drugs would not be administered unless there was evidence that the patient had had embolic phenomena or because of the appearance of varicosities or phlebothromboses it seemed likely that he might have an embolic accident Should they be administered they would be administered as in the outline given above The patient would be given 1 ounce of petrosyllium three times a day until the stools were loose and mushy The dose would then be adjusted to maintain a loose stool Digitalis would be administered in the method as outlined above In the patient weighing 180 pounds and not acutely ill we would give the patient digitora grains 1 28 four times a day for 4 days, and three times a day for 3 days and then if not digitalized he would receive one tablet three times a day until fully digitalized When digitalized he would receive one or two tablets daily to maintain the digitalization Should he need immediate digitalization and could take the drug orally we would give him digitoxin as outlined above and if he were vomiting cedilanid would be given intravenously as outlined In order to produce diuresis it might be necessary in this patient to give 1 000 cc of 10% glucose intravenously or 25 cc of 25 percent glucose intravenously Morphine sulphate grains $^1/_4$ with atrophine sulphate grains $^1/_{1\ 0}$ would be given as often as every three hours for sedation and to allay apprehension Oxygen would be administered if needed and sedation usually in the form of mebaral grains $^1/_2$ four times daily Immediately when seen he would receive 1 cc of salyrgan theophylline intramuscularly and this would be repeated daily as outlined above Should it be necessary to bleed the patient this would be done or if necessary mechanical removal of fluid by the use of paracentesis thoracentesis or the Southey tubes would be instituted The treatment would be continued until the heart had become compensated and then he would continue to get maintenance of digitalis ammonium chloride with restricted fluid intake and the routine use of salyrgan theophylline intramuscularly In addition he would be taught to live within the limits of his compensation and to resume as much productive activity as would be compatible with the restoration of his cardiac compensation

It must be emphasized that the treatment of congestive heart failure is time consuming and depends entirely upon infinite attention to detail remembering always that the success of the treatment is dependent upon the constant supervision of the affected individual by the physician in charge

CHAPTER 46

Direct Vision Intracardiac Surgery By Means of Extracorporeal Circulation for Treatment of Congenital or Acquired Cardiac Disease

C WALTON LILLEHEI M D AND RICHARD L VARCO M D

THE PAST decade has brought forth an im pressive display of clinical achievements in the field of cardiac surgery As recently as 1948 there were only three congenital cardiac lesions then amenable to surgical treatment These were patent ductus arteriosus coarcta tion of the aorta and the systemic pulmonary artery anastomotic procedure for tetralogy of Fallot In effect the interior of the heart represented an important barrier to progress the last anatomic frontier of the many that have confronted surgeons through the genera tions

The recent important advance in cardiac surgery has been the development of the open operation in which the surgeon sees precisely what has to be done within the cardiac in terior and then proceeds to carry out the necessary reparative measures in a dry field unhurriedly

Every advance such as this brings the pos sibility of a fuller life to many who are at pres ent disabled or handicapped The magnitude of these developments can be judged from a consideration of the numbers of patients with congenital and acquired heart disease in the community At present some 50 000 infants are born with congenital heart disease in the United States each year In the world as a whole at present birth rates 2 000 infants arrive every 24 hours with congenital defects of the heart Most of these infants are poten tial candidates for corrective surgery Prob ably three-fourths or more have curable le sions utilizing these currently available open methods and all but a few of the remaining can be assisted through surgery The esti mation of those numbers requiring relief from acquired heart disease is admittedly less ac curate A conservative prediction would be that at least 25 000 individuals yearly in the United States can be benefited utilizing only the present possibilities of surgical treatment

These large numbers of patients emphasize the need for widely acceptable and widely ap plicable methods for detection and treatment of cardiac diseases Lest there be any com placency one need only reflect upon the in escapable fact that at this time more children with intracardiac defects are born each day than are being corrected in a year with pres ent existing facilities This backlog of un diagnosed and untreated patients remains less alarming only because of the high attrition rates for many of these malformations in the first years of life as well as later on

Therefore it is quite predictable that the practice of cardiac surgery and particularly open cardiac surgery will not remain con fined to a few medical centers of the world but on the contrary will continue to grow of necessity at an impressive rate

DEVELOPMENT OF OPEN HEART SURGERY

The experimental work of Gibbon[1] beginning in 1939 focused interest upon extracorporeal oxygenating techniques. A clinical application of his type of pump oxygenator as modified by Dennis[2,3] was attempted at the University of Minnesota in 1951. Both operations were for an atrial septal defect and were unsuccessful. In 1952 Lewis[4] and colleagues successfully for the first time repaired under direct vision an atrial septal defect (secundum type). In this young girl general hypothermia was utilized after the method suggested by Bigelow.[5] Closure of atrial septal defects under direct vision utilizing hypothermia thereafter became regularly scheduled procedures. However despite successes with closure of the secundum atrial septal defects the limitations of time and myocardial irritability for intracardiac work under hypothermia quickly became evident. Attempts made to apply this method to the atrioventricularis communis defects or ventricular septal lesions proved unsuccessful.

In turn Gibbon[6] in 1953 reported the successful repair of an atrial (secundum) defect under direct vision utilizing total cardiopulmonary bypass with the aid of his pump oxygenator. Additional successes with either this type lesion or with ventricular septal defects remained impossible to achieve at that time through use of extracorporeal circulation.

During this period while the use of hypothermia became more common and interest in it grew strong at several institutions including the University of Minnesota research here continued equally vigorously on the development of methods permitting intracardiac surgery at normal body temperature. These efforts were fostered by the growing recognition from many hours spent in the autopsy room dissecting and suturing fresh specimens of congenital heart disease that a longer interval than that available under hypothermia would surely be required for the precise repair of the more complex atrial and all ventricular septal defects. Too the group was acquiring laboratory[7] and a limited clinical experience[8] with the possibilities under inflow stasis. This information bolstered by the azygos flow[9] studies ultimately led to a concept of cardiac and systemic tolerance for much lower perfusion rates than other workers had considered possible and thereby laid a foundation for subsequent developments in this field.

METHODS FOR OPEN HEART SURGERY

CONTROLLED CROSS CIRCULATION

To eliminate some of the already mentioned shortcomings of the then existing methods for intracardiac surgery use of a donor circulation was conceived (Fig 1). This circuit would oxygenate and revitalize the patient's blood. An external pump was added to control accurately the interchange of blood which in volume was reduced substantially based upon the azygos flow experimental studies. This method of controlled cross circulation was believed likely to fulfill the objectives deemed necessary to insure the successful intracardiac repair of the more complex congenital lesions. In its experimental trials it had proved wholly effective.[10] The surgeon had available a prolonged time for working within the open heart and in a relatively blood free field. After extensive testing of these principles and methods in the research laboratory the plan was applied clinically on March 26 1954 for the successful repair of a ventricular septal defect.[11]

Forty five patients were operated upon during 1954 and early 1955 by this method. These results are summarized in Table I. Its use was confined entirely to those patients with complicated defects. Most of the individuals suffered from advanced degrees of cardiovascular impairment. This technique[12-15] made possible for the first time completely corrective surgery for these intracardiac lesions: ventricular septal defects, atrioventricularis communis and tetralogy of Fallot.[16,17] All persons previously afflicted with these anom

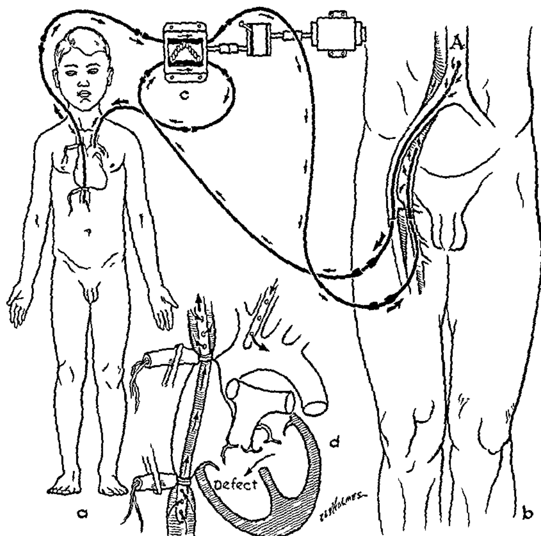


Fig 1 Method for direct vision intracardiac surgery by means of controlled cross circulation
a Patient showing sites of arterial and venous cannulizations
b Donor showing sites of arterial (superficial femoral) and venous (great ... tions
c The pump wh...
d Close up ...
blood from both ...
blood from the c...
clavian artery

alies were either incurable or subjects for palliative procedures only More important perhaps than these initial patients fortunate enough to achieve objective cures for complex intracardiac defects was the fact that this clinical experience with cross circulation clearly indicated contrary to what many had contended that extensive reparative surgery within the hearts of even seriously ill patients was both possible and lifesaving As a matter of fact the technique of controlled cross circulation proved to be physiologically superb for those seriously ill patients Once the circulatory systems of the patient and the donor were

TABLE I

INTRACARDIAC CORRECTION OF CONGENITAL ANOMALIES BY CONTROLLED CROSS CIRCULATION

Results in Patients

Defect	Direct Vision Operative Procedures	No of Pts	Results Successful	Results Deaths
Ventricular septal defect	Suture closure of defect	27	19*	8†
Tetralogy of Fallot	Closure of ventricular defect and correction of pulmonic stenosis	11	6	5
Atrioventricularis communis	Closure of ostium primum with suture repair of atrioventricular valvular deformities	11	1‡	3
Isolated infundibular pulmonic stenosis	Resection of infundibular muscle	1	1¶	0
Pulmonary stenosis, with atrial septal defect and anomalous pulmonary venous drainage into S V C and right atrium	Pulmonary valvulotomy closure of atrial defect and transportation of pulmonary veins to left atrium	1§	0	1
Patent Ductus Arteriosus with Pulmonary Hypertension	Exploratory Ventriculotomy division of patent ductus	1	1	0
Total		45	28	17

* Sixteen patients have been recatheterized postoperatively, and in 12 there is no shunt One of these 12 had both atrial and ventricular cardiotomies for co-existing separate defects Four patients have a residual shunt and in all 4 the pulmonary pressures have fallen Three of these 4 have normal pulmonary pressures postoperatively indicating residual shunt is small

† Six of the deaths were in infants under the age of 2 years

‡ Has been recatheterized and no shunt remains (see Table VII)

¶ Has been recatheterized and the preoperative pulmonary artery pressure of 136/0 mm Hg was (4 mo postoperatively) 25/10 mm Hg

§ An 11 month-old infant

DONOR RESULTS

No of Donors	Early-Late Mortality
45	0

TABLE II

METHODS OF EXTRA-CORPOREAL OXYGENATION UTILIZED IN CONJUNCTION WITH A MECHANICAL PUMP FOR OPEN CARDIOTOMY

(University of Minnesota Hospitals)

Method of Oxygenation	Era Used	No Patients
Controlled cross circulation	1954 1955	45
Perfusion from a reservoir of arterialized venous* blood	1955	5
Biologic (dog lung) oxygenator	1955	5
Artificial oxygenator	1955 to June 1957	240
Total		305

* Drawn from the veins of donors previously warmed arms

linked the invalid was assured a continuous supply of normally oxygenated warmed blood from the healthy donor and also this mutual circulation was constantly undergoing appropriate adjustments through the numerous homeostatic mechanisms of the donor's lungs, kidneys liver, and other organs Both in theory and practice it is unlikely that a technique for total cardiopulmonary bypass will be developed which for the patient's safety, possesses more advantages than this one

Meanwhile stimulated by the demonstrated fact that these more complex intracardiac defects could be corrected work pushed ahead rapidly on the development of non donor blood oxygenators By 1955 the Mayo Clinic group[18] through their modification of the Gibbon machine were able to report clinical successes after intracardiac operations Meanwhile, during 1954 and 1955 from the University of Minnesota cardiovascular research group come three non-donor methods perfusion from a reservoir of arterialized

TABLE III

RESULTS 305 PATIENTS UNDERGOING OPEN HEART SURGERY DURING CARDIOPULMONARY BYPASS WITH TOTAL BODY PERFUSION

(1954 to 1957 (June 1) University of Minnesota Hospitals)

Lesion	*No Cases Treated*	*Survival**	*Mortality %*
Ventricular septal defect	154	109	29
Tetralogy of Fallot—cyanotic			
first operation	60	40	33
previous shunt procedures	5	0	100
—acyanotic	6	5	16 6
Atrioventricularis communis	20	11	45
Atrial septal defect (secundum)	12	12	0
and valvular pulmonic stenosis	1	1	
and pulmonary stenosis (trilogy) cyanotic	3	3	
and pulmonary stenosis, anomalous pulmonary venous connection	1	0	
Isolated pulmonic stenosis—valvular (acyanotic)	3	2	
—infundibular (acyanotic)	1	1	
—atresia (cyanotic, infants)	5	0	
Total anomalous pulmonary venous connection			
Superior vena cava	1	0	
Coronary sinus	2	1	
Ruptured aneurysm sinus valsalva	3	3	
Aortic pulmonary window	1	0	
Complete transposition great vessels	5	0	
Aortic stenosis—congenital			
valvular	1	1	
infundibular	2	1	
Aortic stenosis—acquired calcific	5	3	
Mitral stenosis—congenital	3	3	
—rheumatic	3	2	
Mitral regurgitation—rheumatic	2	2	
Aortic regurgitation—rheumatic	2	1	
Exploratory ventriculotomy (patent ductus)	1	1	
Exploratory ventriculotomy and atriotomy (primary pulmonary hypertension)	1	1	
Aneurysm of aortic arch (resection and grafting)	2	1	
Total	305	204 (67%)	

* Includes operative and late deaths.

blood[14,19,20] (Fig 2) use of a specially prepared biological (dog lung) oxygenator[21] (Fig 3) and a disposable plastic bubble diffusion oxygenator[22-24] The first while practicable for infants provided for larger patients too brief a duration of bypass with any reasonable sized reservoir The second while successful in its clinical oxygenation of human blood would unpredictably develop pulmonary edema to the extent that its usefulness was limited Since early 1955 the method of choice in this clinic for patients requiring open cardiac procedures has been the artificial oxygenator of a simple disposable, bubble diffusion type The same type pump utilized initially with controlled cross circulation has continued to prove satisfactory The number of patients treated utilizing each of these oxygenating methods has been summarized in Table II

CARDIAC LESIONS MANAGED BY OPEN CARDIOTOMY

The availability of effective methods for working within the open heart has permitted the application of visual repair to an ever increasing variety and number of congenital and acquired malformations of the heart

This report, based upon 305 such operations reviews the present status of open heart sur

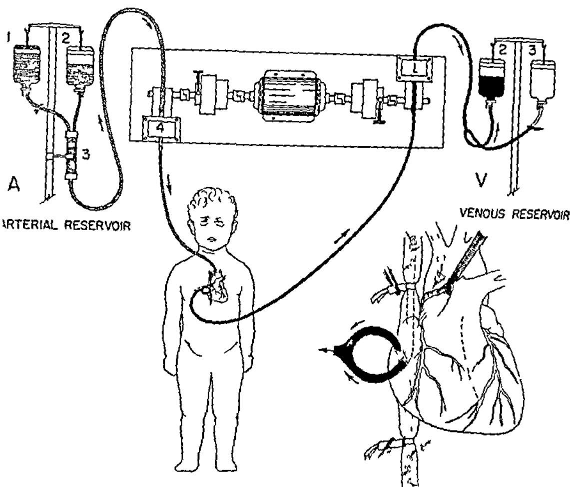


Fig 2 Arterial reservoir perfusion
Extracorporeal circuit A The arterial reservoir showing the bottles of arterial blood (1 2) blood filter (3) and arterial pump (4) V The venous portion of the perfusion circuit with the venous pump (1) and the empty bottles (2 3) for the collection of the venous blood withdrawn from the patient s caval system At the top center is the pumping assembly The patient s relationship to the system is depicted in the center of the diagram In the lower right is a close up view of the cannulations about the patient s heart *Note A Rumel tourniquet has been placed about the base of the aorta* in order to insure a dry intracardiac field by intermittent occlusion as needed

ry at the University of Minnesota Heart Hospitals

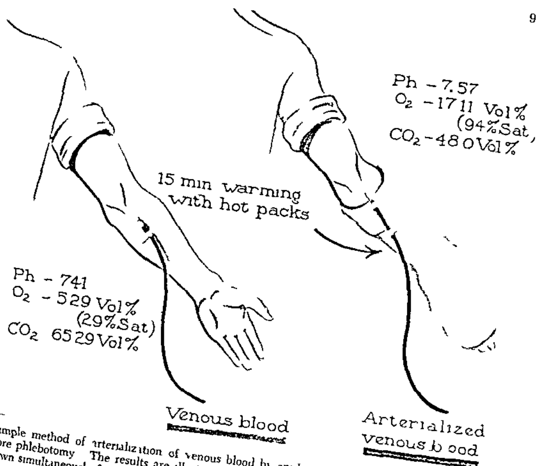
Those lesions so managed are summarized in Table III

CARDIOPULMONARY BYPASS—PRESENT TECHNIQUE

The standard technique for total cardiopulmonary bypass is diagrammed in Figure 4 The patient s venous blood is allowed to flow by gravity from the caval cannulae into a plastic reservoir (not shown in figure) and then is pumped into the oxygenator† The venous blood rises on the oxygen column through the vertical mixing tube and after debubbling occurs it is moved by gravity into the helix reservoir This blood now arterialized is returned through filters by the arterial pump to the patient s arterial system All of the catheters the tubing* and the oxygenator itself are of polyvinyl plastic They are steam sterilized in an autoclave and are discarded after a single use The connectors adaptors

* The tubing actively compressed by the pumping Sigmamotor fingers is of pure gum rubber the remaining portions are polyvinyl plastic

† Made by the Phelan Hospitals Supply Company Minneapolis Minn



B Simple method of arterialization of venous blood by application of cutaneous heat to donor's arm before phlebotomy The results are illustrated for a representative study in which blood samples were drawn simultaneously from the normothermic and the warmed arms of the same individual

are polished stainless steel[7] and are reused after appropriate cleansing and sterilization

During the perfusion interval blood aspirated from the interior of the heart and operative field is returned directly to the oxygenator by the low pressure cardiotomy sucker system described elsewhere [41 42]

For congenital malformations such as ventricular septal defects tetralogy of Fallot, and pulmonary stenosis surgical exposure is by means of a midline sternotomy After dividing the sternum the internal mammary artery is exposed and proximally cannulated with a small polyethylene catheter and connected to a recording device to provide conveniently a continuous record of arterial pressure Upon opening the pericardium the superior mediastinum is inspected for a left superior vena cava In all patients with pulmonary hypertension due to congenital heart disease the ductus arteriosus area is dissected out routinely to determine patency Both of these congenital anomalies are frequent associated defects (Table V) and interfere with perfusion if they remain undetected For lesions confined to the aortic valve the midline sternotomy gives excellent exposure For acquired heart disease of the mitral valve surgical exposure is obtained through a right thoracotomy with the patient in a lateral position This same incision is utilized for combined lesions of the mitral aortic and tricuspid valves For such congenital defects as atrial septal defects atrioventricularis communis and certain forms of total anomalous pulmonary venous connection the surgical exposure is often obtained either through a right thoracotomy with the patient in the lateral position or a bilateral an

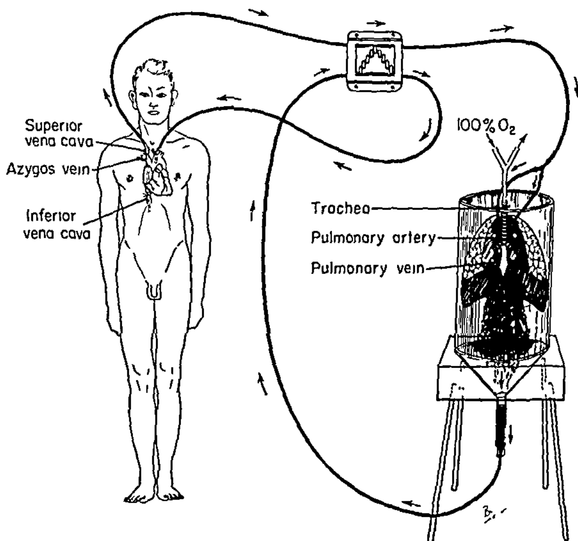


Fig 3 Biologic Membrane oxygenator The circulation utilizing a heterologous (dog) lung for oxygenation of the patient's blood Note The pulmonary veins of the heterologous lung are not cannulated but allowed to drain openly to minimize the occurence of pulmonary edema

terior thoracotomy incision Specially designed thin walled plastic catheters* are used for the vascular cannulations The outflow from the superior and inferior venae cavae is obtained by transauricular insertion of these catheters To insure the completeness of this return during cardiac bypass the cotton tapes which have been previously placed around the cavae and passed through a short length of rubber tubing are tightened around the caval cannulae by cross clamping this rubber sleeve (Fig 2) A plastic catheter into either of the subclavian arteries or the femoral artery serves for return of the arterialized blood At the end of the bypass procedure the subclavian artery is ligated in infants and smaller children and repaired in adults A femoral arteriotomy which is preferred for most open heart procedures is always repaired

Just before insertion of these great vessel catheters the patient is heparinized (1 5 to 2 mg /kg body weight) and after their removal polybrene (2 to 3 mg /kg body weight) is given to counteract the heparin In these heparinized patients hemostasis must be more meticulous With rigid attention to this de-

* Bard c Card ovascular catheters C R Bard Inc Summit N J

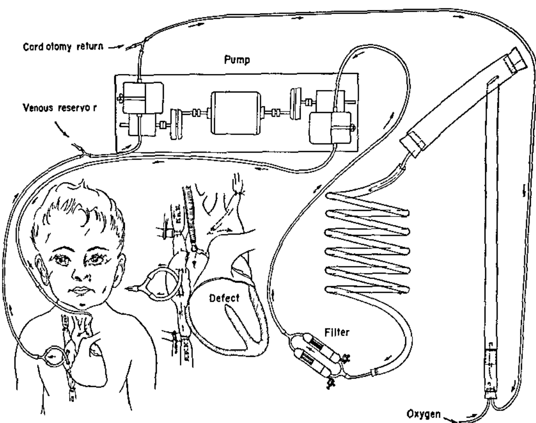


Fig 4 Diagram of extracorporeal circulation during total cardiopulmonary bypass utilizing the helix reservoir bubble oxygenator with sigmamotor pump

tal hemorrhage has not been a problem except in unusual circumstances

The pump-oxygenator is primed with heparinized blood usually drawn within 24 hours of use Heparinized blood is used for any replacement needed during the actual perfusion Before and after this interval citrated blood is used

The patient s body temperature is monitored by a recording rectal catheter Specific efforts are made to keep body temperature at normal levels during the entire operation so as to avoid the depressing effects of systemic hypothermia upon the myocardium or the increased oxygen demands of hyperthermia The temperature control is effected by warming the blood in the arterial reservoir of the oxygenator to 41°C thru use of a water bath and by placing a mattress under the patient through which either heated or cooled fluid may be circulated

During operation all patients are monitored by a portable electroencephalographic recorder (Fig 5) as well as a continuous recording of systemic blood pressure

BUBBLE DIFFUSION PUMP OXYGENATOR

For intracardiac surgery we have had our greatest experience with the bubble diffusion oxygenator This has proven a simple yet very efficient apparatus in which venous blood is filmed directly upon the surface of large bubbles of the oxygenating mixture (100% oxygen) This process creates a large blood oxygen surface area which is in intimate contact for the rapid interchange of oxygen and carbon dioxide as the blood gently rises in the mixing tube Foam formation at that time is undesirable and is evidence of improper technique Next arterialized blood spills into the silicone coated plastic walls of the debubbling chamber Simultaneously the excess carbon dioxide and oxygen escape and the arterialized

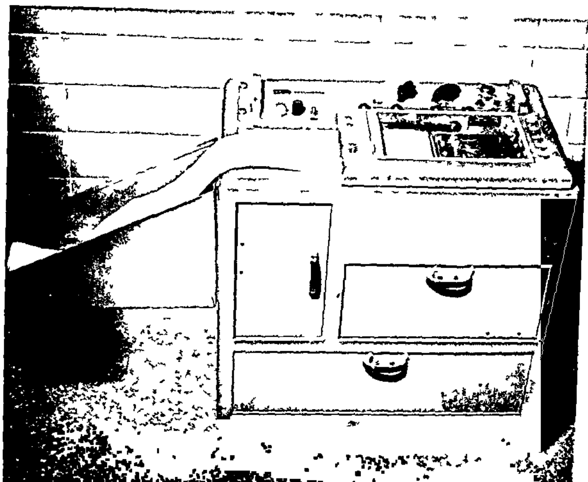


Fig 5 The portable electroencephalograph This machine is used routinely in the operating room to record the patient's brain wave pattern continuously during the bypass interval

blood descends by gravity flow into the helix reservoir Figure 6 portrays this apparatus which has been utilized in the majority of the patients herein reported

UNITIZED DISPOSABLE SHEET OXYGENATOR

Both because of its simplicity and satisfactory performance the helix reservoir bubble oxygenator was adapted in principal to produce a model suited to commercial production in quantity The attainment of this objective should facilitate the development of open cardiac surgery not only in those centers where it is already being used but also assist in the growth of this technique in many other areas with less experience solving the equipment problems inherent in this type of surgery This unitized oxygenator [5 43] is constructed from two sheets of polyvinyl plastic The desired channels and chambers are delineated by a heat seal (Fig 7) The same chambers are present as in the three dimensional prototype vertical mixing tube a siliconized debubbling chamber and a series of inclined settling columns The oxygen disperser is heat sealed into the lower end of the mixing chamber and a saran filter has been fabricated into the arterial exit from the settling chamber Two venous inflow tubes enter the lower end of the mixing tube One accepts *venous inlet to the oxygenator from the cavae* and the other tube carries the return flow from the cardiotomy aspirator

ELECTIVE CARDIAC ASYSTOLE

The use of cardioplegic agents to stop temporarily the beat of the heart with con

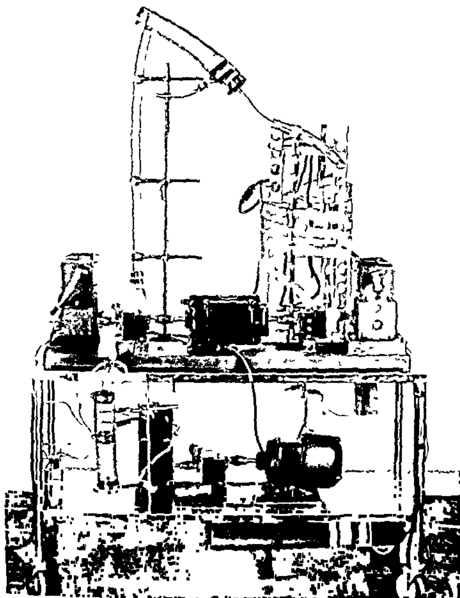


Fig 6 The helix reservoir pump oxygenator utilized for direct vision intracardiac surgery

The pump consists of a single explosion proof electric motor which activates two pump heads (arterial, venous) each equipped with an individual speed changer all mounted on a single base The artificial (large bubble) oxygenator has no moving parts, is sterilized by autoclaving, and is constructed entirely of polyvinyl plastic tubing which is discarded after each perfusion From left to right may be noted the vertical mixing tube, the transverse debubbling chamber, and the helix reservoir immersed in a constant temperature water bath From the lower end of the helix the oxygenated blood is returned thro [illegible]

t[illegible]

T[illegible]

[illegible] from the open heart is seen on the lower level

This pump-oxygenator has been utilized now by us in more than 600 patients

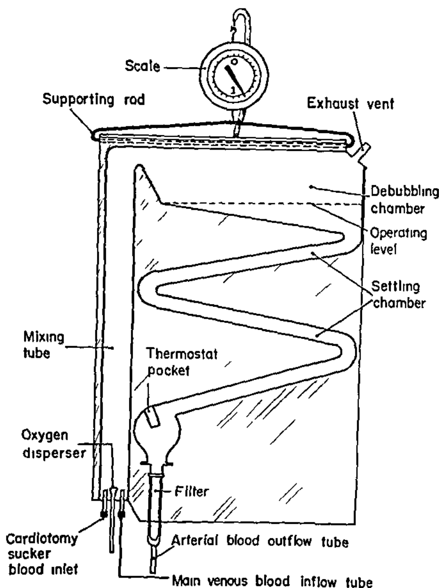
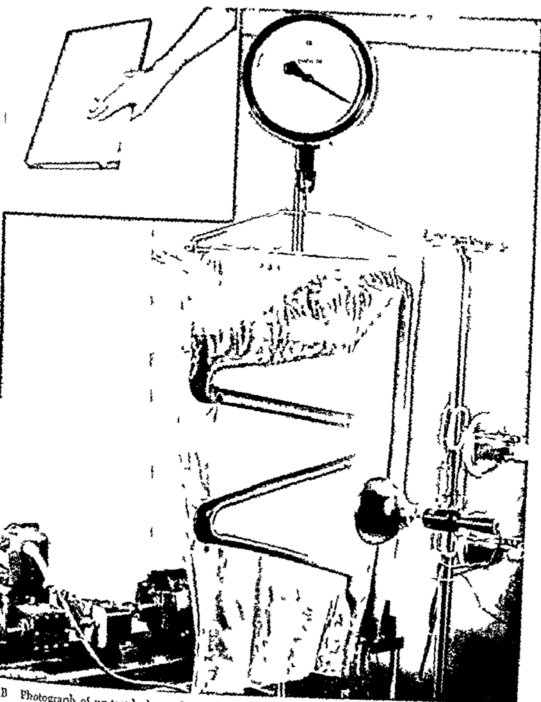


Fig 7 A Diagrammatic illustration of the disposable plastic sheet oxygenator suspended from the spring scale

comitant clamping of coronary arterial flow allows full realization of one of the major goals of open heart surgery namely an operative field that is both dry and motionless We have used potassium citrate for this purpose in 43 patients and acetylcholine in 2 of the patients in this series

This remedy has proved most useful in those septal defects where exposure of the pathology is found difficult We have not used potassium asystole routinely but rather selectively because of the morbidity (increased incidence of heart block) and mortality (inability to restart two hearts* after only brief arrest of less than 11 minutes) We have preferred to make this decision after the heart has been opened and the pathology inspected[10] The use of cardioplegic agents for acquired lesions of the mitral or aortic valves is hazardous and contraindicated in the present state of our knowledge More recently the use of selective cardiac arrest by hypothermia (perfusion of the coronary arteries with blood from 5° to 12°C) has superseded the use of potassium citrate

* Both patients had aortic valve disease with marked ventricular hypertrophy



B Photograph of unitized disposable bubble oxygenator of plastic sheet in combination with the ...rmamotor pump during perfusion. Note: The suspending spring scale which allows instantaneous ...ssessment of the blood volume. Heat loss is being controlled by the three heat lamps directed on ... settling chamber. These lights are automatically turned on and off as necessary by the simple ...rmostatic relay switch inserted in the special pocket.
Inset: This oxygenator is available as a sterile packaged unit ready to hang up, prime, use and then ...discarded.

RESULTS OF OPEN CARDIOTOMY

These efforts have been directed primarily toward the correction, and even cure, of previously inoperable lesions As a consequence, many of the patients have been seriously ill prior to surgery Patients with correctable lesions, we believe, deserve the potential benefits of surgical treatment, even though the calculated risk may be high *in some seemingly* hopeless clinical conditions For instance, one 8 week old *infant, with only a clinical* diagnosis (correct) of ventricular septal defect, was operated upon, using the pump-oxygenator, as an emergency night-time procedure because the cardiologist was convinced that under medical management she could not survive until morning Obviously, any group's enthusiasm for accepting these extra bad risk cases from among patients uniformly quite ill of their disease, will be *an important* determinant in survival rates Moreover, much *learning was necessary in the beginning by* the inevitably painful method of trial and error The *in vivo* problems of unfamiliar or poorly described pathological malformations has demanded on-the-spot improvisations which, naturally, did not always succeed the first time These facts are, of course, paramount in evaluating the successes obtained as well as the failures recorded

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect is a common congenital cardiac malformation, and it probably even exceeds patent ductus arteriosus in incidence It has been the most frequent lesion in this series (154 patients) Nevertheless, prior to March of 1954 this defect was incurable, although in the past there has been little question of the desirability of closing all ventricular septal defects and particularly *those associated* with pulmonary hypertension (which includes the vast majority) Of all *patients born* with a ventricular septal defect, in the times prior to corrective surgery, most died *of the consequences of their defect*, and many succumbed in the first year of life Those *surviving this hazardous initial twelve months* dwindle rapidly in number, and only a small percentage reach the teens *Only two* patients in this operative series of 154 patients were older than 15 years (18 years and 38 years, respectively). Death of the patient, and not factors of case selection, we believe, are responsible for this revealing fact In our experience *many of the older patients were* carried in our clinical records for years as "*typical" ventricular septal defects* or Eisenmenger's complex However, upon surgical exploration they were found to have a variant such as truncus arteriosus, "corrected" transposition[14] of the great vessels, or one of the several forms of single ventricle with or without transposition The finding of an isolated ventricular septal defect in these older patients certainly occurs, but is unusual The conclusion is inescapable that a very limited number of persons born with an isolated ventricular *septal defect ever survive* beyond the pediatric age group unless cured surgically

The lethal element of ventricular septal defects is, primarily, the early, rapid, and progressive development of pulmonary hypertension associated with a high pulmonary vascular resistance From this it is evident that both the pulmonary pressure and the pulmonary flow must be evaluated to assess the pulmonary vascular resistance Patients with an increased pulmonary pressure and a high pulmonary blood flow have a low resistance, i e, are free of significant occlusive arteriolar disease and are good operative risks On the contrary those with a high pulmonary artery pressure but with a modest increase in pulmonary flow usually have a more serious degree of occlusive arteriolar disease and their immediate hemodynamic readjustment after corrective *surgery is considerably* more difficult

The relatively fewer patients with normal or *moderate elevation of their pulmonary* pressures are, in contrast to patients with high *pulmonary pressures, more susceptible to* bacterial endocarditis prior to corrective surgery The risk for the latter procedure is *low when* pulmonary vascular pressures (resistances) are low Marked elevation of the pulmonary vascular resistance has been the most important single factor determining the operative risk

We believe that the most potent stimulus to

TABLE IV

RESULT OF VENTRICULAR SEPTAL DEFECT REPAIR ACCORDING TO AGE AND DEGREE OF PULMONARY HYPERTENSION

(154 Cases—71 Male 83 Female)

Age Range Years	No Pts	Pul Art Syst Press More than 70% Aortic Syst Press		Pul Art Syst Press Less than 70% Aortic Syst Press		Total Mortality
		No Pts	Deaths	No Pts	Deaths	
0-1	24	15	9 (60%)	9	3 (33 3%)	50%
1 2	27	12	4 (33%)	15	4 (26 6%	29%
2 5	40	26	11 (42%)	14	1 (%)	30%
5 10	43	21	7 (33%)	22	1 (4 5%)	18 7%
10 20	19	12	4 (33%)	7	0 (0%)	20%
20 38	1			1	1 (100%)	100%
Totals	154	86	35 (40 7%)	68	10 (14 8%)	29 3

Note In the 44 patients over the age of 2 years and with pulmonary hypertension not exceeding 70% of the aortic there were only 3 deaths (6 8%) and each of these 3 patients had a significant associated lesion (see text)

intimal arteriolar proliferation and medial hypertrophy in the patient with a ventricular defect is *not* the increased blood flow through the lungs Patients with atrial secundum type defects often have left to right shunts of a far greater volume than do those with ventricular defects Yet the level of pulmonary hypertension is usually lower and appears later Rather, the initiating and determining factor causing the increased vascular resistance is the systolic thrust of the left ventricular output delivered undamped to the long vessels which provokes proliferative changes

Results

One hundred fifty four patients have been operated upon for closure of a ventricular septal defect in the period 1954 to mid 1957 * The sex distribution was about equal (71 males and 83 females) As indicated in Table IV 45 died creating an over all mortality of 29 3% The type of bypass does not appear to have significantly influenced these mortality rates (Fig 8) However the adverse consequences of infancy and the advanced degrees of pulmonary hypertension on mortality rates are illustrated in Figure 9 Children under 2 years have been poorer operative risks as a group because of the respiratory problems encountered both pre and postoperatively The

* Subsequently to January 1959 109 additional patients with ventricular septal defects have been operated upon with only 11 deaths (10%) despite the fact that indications for reparative surgery in the presence of severe pulmonary hypertension have been progressively broadened

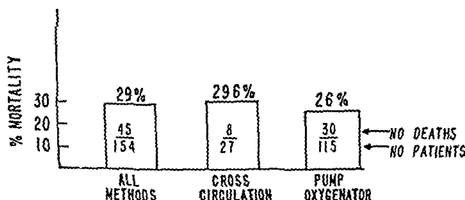


Fig 8 Comparison of results with different methods for extracorporeal oxygenation in patients with ventricular septal defects treated by direct vision closure (1954-1957 series)

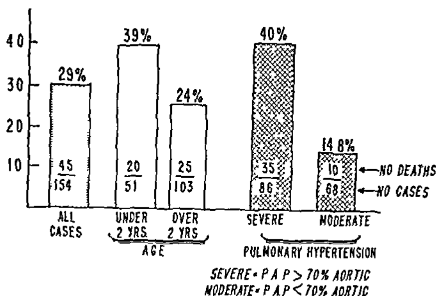


Fig 9 Influence of age (infancy) and pulmonary hypertension upon operative risk for patients undergoing ventricular defect closure (1954-1957 series)

management of secretions their retention and avoidance of pneumonitis is difficult in these tiny infants often weak and underweight from their cardiopulmonary disease The muscular development in the chest wall of even healthy infants is feeble compared to that found in older children

The pulmonary pressure is significant only as a reflection of the degree of pulmonary vascular proliferation Specifically, an individual patient with high pulmonary artery pressure may have either healthy or severely damaged pulmonary vasculature Inherent difficulties arise in the accurate measurement of pulmonary blood flow and the calculations for resistances therefore have less prognostic significance than if they could be precisely measured for the individual patient On the other hand a close correlation has been found to exist between the microscopic appearance of the lung vessels and operative risk.[7] If the pulmonary artery systolic pressure is plotted as a percentage of systemic systolic pressure the frequency of severe pulmonary vascular changes follows the approach of the pulmonary pressures toward systemic levels However it is probable that the incidence of Grade III vascular lung changes does not become universal until these individuals demonstrate a reversal of their shunt (at rest) Many patients with ventricular septal defects die from other causes before this state is reached Thus the accurate evaluation of operative risk in a particular patient with a high pulmonary pressure from the clinical and catheterization data is often difficult Lung biopsy although cumbersome in other respects has been the most accurate prognostic test in our experience

Figure 10 portrays further the interplay of these factors of pulmonary hypertension and age upon risk Noteworthy are the 44 patients beyond the age of 2 years and with considerable but not advanced pulmonary hypertension who underwent corrective surgery with a risk of only 6 8% In fact each of the three patients in this category who died had a serious additional defect or lesion responsible for their demise as follows

Case A aged 2½ years had a large left superior vena cava which was not recognized until after cardiotomy Considerable blood loss occurred before it was located and clamped This patient failed to awaken postoperatively and it is not known for sure whether clamping this large cava with consequent cerebral congestion or the blood loss was responsible for her neurologic injury

Case B a 38 year old woman died suddenly

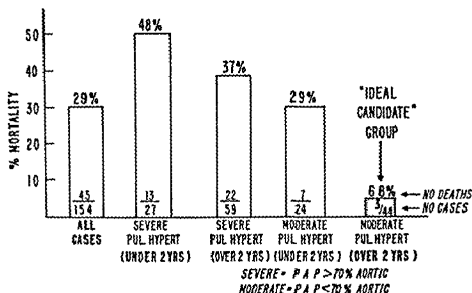


Fig 10 Mortality rates according to degree of pulmonary hypertension and age (infancy) in patients undergoing closure of ventricular defects The pulmonary hypertension is graded on the basis of whether the pulmonary artery systolic pressure is greater or less than 70% of the aortic systolic pressure (1954 1957 series)

while out walking 6 weeks after corrective surgery Autopsy disclosed death was due to a coronary thrombosis in remarkably diseased arteries Her defect closure was completely healed

Case C a 6 year old boy, had severe aortic insufficiency with a small ventricular defect Preoperatively he was thought to have a ruptured aneurysm of sinus of Valsalva At surgery his heart was arrested for only 4 minutes with potassium citrate and it was impossible then to restart it

This "ideal candidate group" is presented not with the implication that corrective surgery should be restricted to these fortunate few (28% of the total series) but rather to forecast for the future the low risk that may be anticipated for this malformation as the problems associated with pulmonary hypertension are mastered In the series of patients operated upon subsequent to those herein reported this predicted substantial reduction in mortality for those afflicted with severe pulmonary hypertension has materialized in a large part[45,46] From Figure 10 it might be deduced that patients under 2 years should best be deferred until older Whether this assumption is valid or not depends on the number dying during this waiting period and unfortunately accurate information on this point is difficult to obtain at present

Associated congenital cardiac defects have been frequent among these patients and probably have influenced the mortality to some extent (Table V) In any patient with a suspected ventricular septal defect and in whom the catheter fails to enter the pulmonary artery, the presence of corrected transposition[44] should be considered and angiocardiography performed

TABLE V

Other Cardiovascular Anomalies Encountered in 154 Patients With Ventricular Septal Defects

Lesion	*No*
Patent ductus arteriosus	22*
Left superior vena cava	16
Endocardial fibroelastosis	8
Atrial septal defects	6
Multiple ventricular defects	6
Coarctation of the aorta	4*
Mitral stenosis	3
Double aortic arch	1
Dextrocardia	1
Aortic regurgitation	1
Corrected transposition	1

* Three patients had a patent ductus arteriosus and a coarctation of the aorta in addition to a ventricular septal defect.

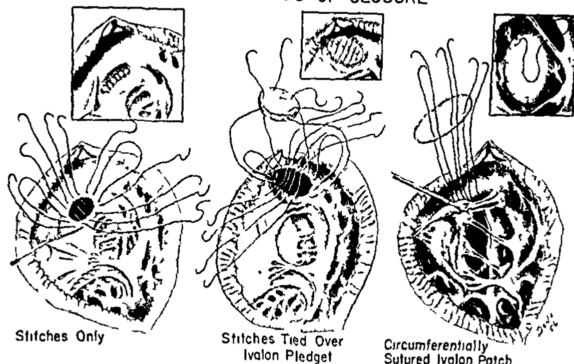


Fig. 11. The methods of closure of ventricular septal defects. Silk (3-0) with a double armed swedged on needle was the suture material utilized in all instances. The Ivalon (polyvinyl sponge) has been compressed 5 to 1 before use. In general the size of the defect and the character of the margins have determined the type of closure, i.e., the smaller holes are closed by stitches only whereas the larger lesions are closed by a circumferentially sutured patch.

INDICATIONS FOR REPARATIVE SURGERY

Because ventricular septal defects are a common lesion and since many die of their defect in the first 12 months of life, a number of the cases seen are in rather desperately ill infants. They suffer from a failure to gain weight, repeated respiratory infections and recurrent or persistent cardiac decompensation. Virtually all already have severe pulmonary hypertension provoked by mechanisms cited. We consider these persons in urgent need of surgical relief but recognize their increased operative risk. They are often destined for an early death unless successfully operated upon. On the other hand, an infant with a ventricular septal defect who gains weight at relatively satisfactory rate and who appears to be responding well to non-operative management we would prefer to postpone surgery if possible until at least age 2. The technical aspects of the defect closure during infancy are not excessive. The major hazards hinge about management of their respiratory complications. However, undue procrastination about an operation during early childhood pyramids the risk for the pulmonary artery pressures in some patients can double within 12 months. The onset of severe pulmonary hypertension is an ominous

TABLE VI

Location and Methods of Surgical Repair of Ventricular Septal Defects in 154 Patients

No.	Location	Ivalon Pledget*	Suture Only	Ivalon Patch†
133	Membranous	58	42	33
11	Posterior	5	3	3
8	Anterior	4	2	2
7	Muscular	3	4	
1	Traumatic		1	
160‡		70	52	38

* Held in place by silk sutures.
† Circumferentially stitched in place.
‡ Six patients had multiple ventricular defects.

sign and indicates that although correction is still indicated the most favorable moment for this surgery has passed. The anatomic locations and brief reference to the type of surgical management for the defects in these 154 patients are summarized in Table VI and Figure 11. A more complete description of the anatomy of these defects has been presented previously.[28]

In summary, it is clear that a ventricular septal defect is a most grave congenital cardiac malformation. It is certain to shorten the life expectancy of most all of those individuals unfortunate enough to have that problem. Closure of the abnormal opening no longer remains the major problem. For those with mild to moderate degrees of pulmonary hypertension this can be done with low risk to the individual. Currently[45,46] important strides are being made in the development of effective methods for managing the complications associated with advanced pulmonary arteriosclerosis in these patients.

POSTOPERATIVE RECATHETERIZATION

Recatheterization has been carried out in 36 of the 109 survivors at an interval of 4 to 16 months after operation. In 28 of the 36 patients no evidence of a left to right shunt was found and the defects were deemed closed. Moreover 25 of these 28 exhibited both a significant drop in the pulmonary artery pressure (averaging 38 mm. Hg systolic) and a fall in pulmonary blood flow of 6.5 liters per square meter per minute (average). The remaining 3 showed no drop in their pulmonary hypertension 1 year after surgery although their calculated pulmonary blood flows had decreased. Their pulmonary arteriolar changes may well be static or progressing and hence these obliterative arterial processes can be self sustaining in a few individuals. This evidence can be construed as yet another reason for earlier operations. Unfortunately all 3 of these cases were done early in the series prior to the time when lung biopsies were more regularly secured. Two of these patients have symptoms. Of the 8 patients with demonstrable left to right shunts on recatheterization 5 now have a normal pulmonary artery pressure. Clinically they are well and hence it is likely that the remaining ventricular defect is small. The other 3 patients each possesses a free ventricular communication with no demonstrable hemodynamic or clinical improvement after surgery.

Thus 35 of the 38 patients (92%) restudied have benefited substantially from their operative procedure. Most of them were operated upon early in our series. In view of the technical improvements since the future possibilities are good for a cure rate even closer to 100%.

ATRIOVENTRICULARIS COMMUNIS

This is a complex defect in which the pathologic variations occupy wide spectra. The complete form encountered in 9 patients in this series consists of an ostium primum atrial septal defect, mitral regurgitation due to a cleft in the aortic leaflet of this valve, tricuspid insufficiency because of a similar deformity of the septal leaflet and a ventricular septal defect from failure of these leaflets

TABLE VII

Atrioventricularis Communis Defect

Cardiac Catheterization Studies Before and After Corrective Surgery*

L. S.
Pre-op catheterization Age 6 mo. 11/9/53
Corrective Surgery 8/6/54
Post-op catheterization Age 19 mo. 12/3/54

Site	Oxygen % Saturation Pre-op	Oxygen % Saturation Post-op	Pressure mm. Hg Pre-op Quiet	Pressure mm. Hg Pre-op Crying	Pressure mm. Hg Post-op
Inferior vena cava	37	[illegible]			
Superior vena cava	12	75			
Right auricle	63	78	3		3
Right ventricle	77	70	55/0	80/10	22/4
Pulmonary artery (trunk)	67	78	55/30	90/50	20/[illegible]
Femoral artery	[illegible]	98.5		135/70	90/50

* Courtesy Dr. J. D. Keith, Toronto. Follow-up examination in January 1959 disclosed a completely normal girl with no cardiac murmurs and normal heart size.

to attach firmly to the ventricular septum This complete form is encountered most often in infants because it usually leads to the early development of severe pulmonary hypertension serious clinical disability and a shortened life expectancy unless relieved by corrective surgery

The partial type that we have encountered most frequently (7 patients) has been an ostium primum defect in association with a cleft mitral a normal tricuspid and no ventricular component

Three patients have had a rather atypical form in which a left ventricular right atrial shunt arose through a defect between these chambers It would appear that these instances represent an embryological variant The tricuspid septal leaflet was cleft in all but the mitral was normal in two

One patient had only an ostium primum without apparent valvar deformity

The atrioventricularis communis group of defects cannot be corrected by blind or closed methods Moreover under hypothermia insufficient intracardiac time is available to deal with this complex With perfusion techniques however precise suturing can be accomplished and cure now becomes possible Repair consists of closure of the septal defects together with careful correction of the valvar malformations Our first patient to have these defects (complete form) corrected successfully was operated upon August 6 1954 through a right atrial cardiotomy utilizing controlled cross circulation [12,13] The preoperative and postoperative catheterization studies upon this infant are contained in Table VII She has remained asymptomatic in the subsequent years [17]

Twenty patients ranging in age from 6 weeks to 29 years with atrioventricularis defects have been operated upon with 9 deaths This relatively high risk rate in the beginning was compounded from several factors slowness in development of a clear understanding of the complex anatomical variables which permits the surgeon to recognize promptly the particular lesion present the frequent development during the operation of complete heart block and the advanced disability of some of the patients accepted for surgery With an increasing experience most all of these ill effects have been overcome Moreover 3 of these deaths were in patients cyanotic at rest Each had systemic arterial pressure levels in the pulmonary vessel Patients with such advanced lesions are not good candidates for corrective surgery The treatment of complete heart block by use of isopropyl levoarterenol (Isuprel)[29] and a pacemaker electrode[30] implanted directly into the myocardium has reduced greatly the mortality from this vexing complication As a result of these additions to our knowledge the operative risk has fallen significantly as evidenced by the frequency of success among recent cases

ATRIAL SEPTAL DEFECTS

The only acceptable treatment for an atrial (secundum) septal defect is one that produces a cure It follows therefore that the results of all forms of treatment closed or open must be appraised after postoperative catheterization An initial low mortality while obviously essential is not all meaningful in an ultimate evaluation of the best method for treating this lesion if many of the patients are not cured Most patients with atrial secundum defects unlike those seriously ill from ventricular septal defects will survive a thoracotomy and exploratory cardiotomy even though their opening may not have been completely closed or even substantially reduced in its diameters Advocates of the various closed methods for "repairing" atrial septal defects have rarely presented postoperative catheterization data Such information as is available reveals a substantial incidence[31] of residual shunts Moreover another consideration is the difficulty of distinguishing preoperatively in all cases between atrial secundum defects and the various forms of the ostium primum syndrome Although many authors have described criteria for making this differential and these signs are of value suffice it to say that accurate differentiation is not possible in every case despite the considerable skill and experience of these diagnosticians As a result in a certain number of patients when utilizing hypothermia or one of the above mentioned blind techniques

for closure of atrial septal defects the surgeon will find himself in the operating room with the patient's chest open and at the mercy of the more complicated pathology unexpectedly found to be present

This is true because, as already stated, it is possible to deal curatively with the atrioventricularis communis defects (ostium primum syndrome) only if one has available a pump oxygenator and total cardiopulmonary bypass With hypothermia or a closed method the patient in this situation is doomed either to failure or at best if he survives to a thoracotomy which not only served no purpose but actually has impaired his chances for successful curative surgery at a later time using cardiac bypass because of the additional hazards induced from vascular adhesions when he is reoperated upon and heparinized These considerations are sufficiently vital to the patient's well being to advocate the use of total cardiopulmonary bypass with the pump oxygenator for repair of all atrial septal defects The dividends of this policy have been numerous*

First, in the small series of 12 patients ranging in age from 2 to 51 years with atrial secundum defects there have been no deaths The ability to close even these simple defects in an unhurried and precise manner with interrupted stitches indicates that the percentage of anatomic cures may be expected to approach 100% And finally we have encountered unexpectedly complicated secundum defects that could be repaired completely with ease In one such patient with unsuspected drainage of the right pulmonary veins into the superior vena cava and a foramen ovale defect the repair although straight forward required a bypass interval of 55 minutes to avoid encroachment by the repair upon these venous channels Moreover we have encountered an ostium primum lesion in several instances where even after retrospective study there was no reason to suspect more than a secundum lesion

It is quite predictable that other cardiologists and surgeons will as they acquire confidence in their pump oxygenator, abandon completely the less satisfactory methods that have been advocated in the past for closure of atrial septal defects

* As of January 1959 41 patients have had atrial defects repaired utilizing the pump oxygenator with one death (2.4%) Ten patients have had post operative catheterization and all are cured

TETRALOGY OF FALLOT

The Blalock Taussig anastomotic operation or the Potts modification has in the decade or more since their introduction brought effective palliation to the lives of many previously crippled from the physiologic abnormalities associated with Fallot's tetralogy

Inevitably however because this procedure is by function palliative the mortality and morbidity continue to rise at an abnormal rate with the elapse of time The magnitude of this increased attrition was charted in a follow up study recently completed for all of the patients having had the systemic pulmonary artery shunt performed at the University of Minnesota Hospitals during the years 1946 to 1954 (Table VIII) Whereas the initial (operative) mortality rate of 9% was about standard the late deaths (21%) have more than doubled this primary risk Furthermore at the time of their check up from 2½ to 10 years after operation in addition to the 30% who were dead another 16% of the patients were unimproved and in need of further surgery

TABLE VIII

TETRALOGY OF FALLOT*
SYSTEMIC PULMONARY SHUNT

University of Minnesota Hospitals
1946 1954

Patient Status January 1957†

Total Patients			110
Died of Operation	10 (9%)	30%	46%
Died Later	23 (21%)		
Unimproved	18	16%	
Improved	62	54%	

* Tricuspid atresia single ventricle transposition cases excluded

† A 100% patient follow up was possible in this series

These late failures recorded with the palliative procedure were most often not related to the closure of a previously functioning shunt but rather to the patient "outgrowing his shunt" This same fact explains why the results of the shunt operation have been generally poorer when performed either in infants or in adults In infants the vessels often are not large enough to permit construction of a satisfactory shunt and in adults are not large enough for the size of the body mass involved

The fact that 54% of this series still remain improved is certainly good evidence of the palliation that was provided by the shunt procedure Its merit is even more apparent when one recalls the outlook for these individuals prior to its offering Rather these follow up studies have served to define for us the area in which improvement is both necessary and possible by means of the completely corrective procedure

The basic defects in Fallot s tetralogy are twofold—ventricular septal defect and pulmonic stenosis Clearly the goal in these patients is the complete correction of all existing defects by open cardiotomy After having thus restored the circulation to normal anatomically and physiologically one can anticipate that life expectancy may be lengthened to its full span Moreover it is apparent that the risk for the individual undergoing curative surgery is limited to the initial operative hazard

Since August of 1954 at the University of Minnesota Heart Hospitals we have not found it necessary to perform any shunt procedures for tetralogy of Fallot cases All patients deemed in need of surgical assistance have had the curative procedure[16,17] (closure of the ventricular septal defect together with pulmonary infundibular resection and/or pulmonary valvulotomy)

The operative indications for the completely corrective procedure have been similar to those recognized as valid for the shunt procedure and consist of definite evidence of deterioration This state may be represented either by recurrent bouts of heart failure (usually in infants) or decompensation of the pulmonary collateral channels (syncopal episodes extremes of dyspnea upon slight effort or a sustained rate of increase in the hemoglobin level erythrocyte count or hematocrit value)

These patients include a number of infants and the youngest a success was 16 weeks old.

With the curative procedure the operative risk has steadily decreased* as experience has been gained with the technical problems involved (Fig 12) It is even likely that the operative risk among tetralogy cases can be less than that for simple ventricular septal defects because the pulmonary circulation in the tetrad group has not been damaged by pulmonary hypertension In that regard a tetralogy patient with a left to right shunt already represents a very low surgical risk Furthermore the completely corrective procedure is technically feasible at all ages from infancy to adults (our oldest patient also successful was 48 years) We have been gratified with the results of postoperative studies finding a drop in the right ventricular pressure without a gradient or with a very small gradient across the infundibular or valvular area into the pulmonary artery (Fig 13) In the 40 tetralogy patients of this series the mean postoperative femoral artery oxygen saturation was 93 7% (87 to 100%) as compared to the mean preoperative value of 51% (19 to 86%)

For the patient with tetralogy of Fallot defects in areas where facilities for open heart surgery are not yet available we currently recommend withholding save for the most desperately deserving any shunt procedure with the hope that a corrective operation can be carried out eventually This philosophy does not deny the risk of complications for certain of these patients Rather it stems from experiences which indicate that the creation of a shunt procedure has enhanced the patient s risk when intracardiac surgery is subsequently attempted (Table III) The bleeding problems from these extensive collaterals and arteriolar adhesions which develop in cyanotic patients who have had thoracotomies are indeed formidable during

* Sixty additional tetralogy of Fallot patients have had complete correction of their defects with an operative risk of 10%

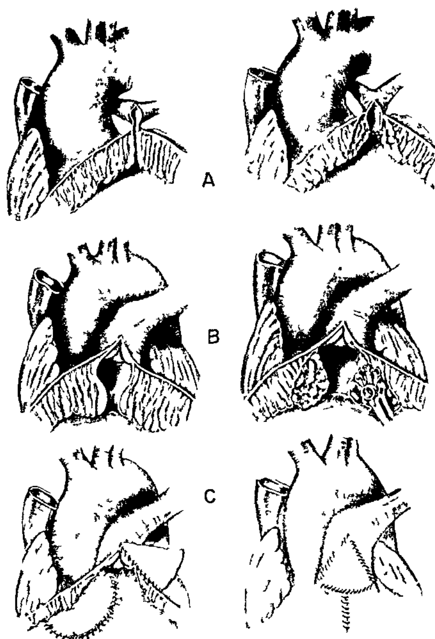


Fig 12 Methods of treatment of the right ventricular outflow obstruction in tetralogy of Fallot A The atretic segment is resected and the pulmonary artery just proximal infundibulectomy which is sufficient in the patients with mild or moderate degrees of obstruction C shows an Ivalon roof used to expand the right ventricular outflow tract in patients with an extreme degree of hypoplasia in this area

COMPLETE TRANSPOSITION OF THE GREAT VESSELS

This common congenital malformation invariably fatal in infancy continues to remain a major challenge to cardiac surgeons After a modest experience with palliative operations[34,35] we abandoned that concept in favor of total correction of all the primary and associated defects This has required total bypass and the pump-oxygenator So far success has eluded us as it has others yet someone with superior ideas is certain soon to identify the proper techniques for overcoming these difficulties

Baffes[49] has recently resurrected with some modification the palliative procedure we described[34] but our experience with it has indicated the obvious advantages of perfecting the techniques for complete correction in one stage utilizing bypass

RUPTURED SINUS OF VALSALVA

Rupture of an aneurysm of the sinus of Valsalva into one of the right cardiac chambers results in a left to right shunt An added consequence is a reduction in the systemic diastolic pressure The characteristic murmur and findings at catheterization make the correct diagnosis relatively likely However selective retrograde angiography may be necessary to separate it from an atypical patent ductus arteriosus[32] aortic pulmonary septal defect coronary arteriovenous fistula or a ventricular septal defect with associated aortic insufficiency

Until recently persons suffering from this lesion either died prematurely or were incapacitated from their progressive cardiac decomposition Since 1956 3 patients (aged 6 to 37 years) with this malformation have been operated upon utilizing the pump oxygenator Successful corrective surgery has been possible in all cases[36] Retrograde perfusion of the coronary sinus was used in one[37] and elective potassium asystole in the other two to permit temporary cross clamping of the ascending aorta during repair

Thus, the advent of bypass techniques has completely altered the hopeless prognosis previously associated with this relatively uncommon lesion

AORTIC STENOSIS

Patients with congenital aortic stenosis requiring surgical relief are best treated by an open method utilizing total cardiopulmonary bypass and the pump oxygenator[38,39,5] When the congenital aortic lesions have been operated upon with closed methods the results were often poor Aortic insufficiency was produced in those with valvular lesions and the surgeon found that adequate relief of any infundibular obstruction of the subvalvar type was difficult to achieve In our own experience these subvalvar intrusions have occurred in 15% of the cases coming to surgery

The direct vision exposure of the valve with acquired aortic stenosis utilizing the pump oxygenator has greatly improved the results of aortic valvotomy A more effective placement of the commissurotomy and freeing of adhesions to the sinuses can be accomplished to mobilize the cusps (Fig 14)

Moreover the valve leaflets in this disease are nearly always rigid scarred and heavily laden with calcium Myocardial involvement is nearly universal in the patients coming to surgical treatment Left ventricular hypertrophy frequently exceeds the available coronary blood supply so that angina pectoris and focal (myocardial) necrosis are frequent even when organic coronary artery disease may be absent Thus the cardiac reserve is generally low moreover the threshold for fatal ventricular fibrillation is likewise low and the patients are often in the sixth decade or beyond All these factors have added up to a challenging and formidable problem to the cardiac surgeon who has sought to improve their lot

Since 1956 the authors have performed all operations for aortic stenosis under direct vision utilizing extracorporeal circulation and as a consequence have come to appreciate the numerous advantages of this approach As experience has grown a major advance has been the development and application of techniques for decalcifying these leaflets in vivo at the time of surgery thus affording a degree

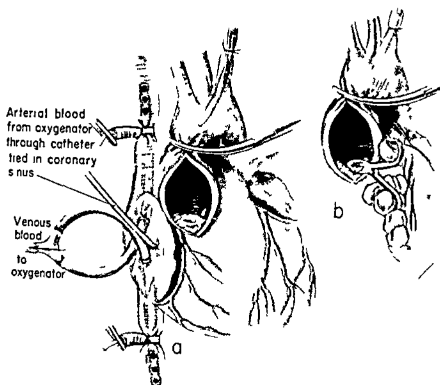


Fig 14 Aortic valvulotomy under direct vision utilizing cardiopulmonary bypass and retroperfusion of the coronary sinus with oxygenated blood The retroperfusion of the veins maintains myocardial oxygenation and prevents coronary arterial air embolism More recently the highly desirable benefits of myocardial oxygenation are maintained by direct coronary artery perfusion with arterial blood from the pump oxygenator selectively cooled to 3° to 10°C (Selective Cardiac Hypothermia)

of flexibility to the reconstructed leaflets not previously thought to be attainable Finally in some patients the aortic valve has been so severely destroyed by the calcific process that attempts at reconstruction have failed and in these a prosthetic aortic valve has been successfully inserted in the normal position proximal to the coronary ostia

A major factor in the success of these technical advances has been the development and application of selective hypothermia of the heart by coronary perfusion These hearts with advanced disease of the left ventricle for reasons already cited endure even brief intervals of hypoxia very poorly, and the use of potassium citrate or acetylcholine asystole without coronary flow is not tolerated as it has been in congenital heart disease where the myocardial reserve is often quite good

For the future it is quite predictable that open techniques will be recognized by all as essential for the treatment of aortic stenosis

AORTIC REGURGITATION

Insufficiency of the aortic valve has presented a formidable challenge to surgical treatment The palliation afforded to certain patients with advanced cases by the insertion of a Hufnagel valve into the descending thoracic aorta has been of definite value However something more curative clearly was necessary

In the past the thought has been advanced by some that nothing definitive could be done



Fig 15 Method of plication of the annulus for mitral regurgitation carried out under direct vision through a left atriotomy The heart and lungs are bypassed utilizing the pump oxygenator The left atrium is exposed through a right postero lateral thoracotomy (a) Mattress stitches of heavy silk are placed in the enlarge annulus (b) and then tied over pillows of compressed polyvinyl sponge (c) As the atriotomy incision is closed the mitral valve is held open (by the instrument) to prevent entrapment of air within the left ventricle

for this lesion until a completely satisfactory prosthetic valve was available—and one that could be inserted so as to replace the diseased valve and lie proximal to the coronary artery ostia We have disagreed with t o phy for several reasons first of a satisfactory valve can only com the result of a greater familiarit pathologic anatomy acquired in pr cal procedures w s area un vision Secondl ear that familiarity was would that methods fo on of valves would ev mplete ficial valve may n early a

as original predictions suggested This predicted sequence of events has already materialized for th ic valve as it did previously in respect to ive surgery

Pathologic f Aortic Regurgitation

One very natomic aspect of the primarily a ient I hat has impressed u hea tudied a the fresh e s of the flet tissue sence leum to the patho with ao

Surgical Correction of Aortic Regurgitation

Emboldened by the experience gained in the correction of aortic stenosis cited above as well as aortic insufficiency occurring after corrective procedures to relieve stenosis we have undertaken corrective surgery in patients with pure aortic regurgitation as a regular procedure [39, 40]

As mentioned above two basic surgical techniques have evolved for the repair of aortic regurgitation under direct vision These are valvuloplasty (reconstruction) or insertion of prosthetic valves and leaflets proximal to the coronary orifices The decision as to which approach may be desirable in a particular patient usually cannot be made until after the aorta has been opened and the pathology has been exposed

In selected instances conversion of the aortic valve to a bicuspid orifice[39] has been very successful in completely obliterating the regurgitant leak without production of stenosis

For all of these procedures total cardio*pulmonary bypass with coronary perfusion by* one of the several technics already discussed has been utilized Cardiac arrest utilizing either potassium citrate or acetylcholine are unsatisfactory for use in patients with acquired aortic valvular disease Normal myocardial oxygenation is essential for success as indicated in the discussion above (aortic stenosis) we now prefer selective cardiac hypothermia by coronary arterial perfusion to best achieve this objective

Follow up *studies on patients with pure* aortic insufficiency treated by these technics have indicated that complete correction of aortic insufficiency has been possible with obliteration of previously present murmurs (normal postoperative phonocardiograms) and correction of all hemodynamic evidence of the leakage as indicated by selective angiography and objective pressure date

Thus pure aortic insufficiency may be added to the rapidly lengthening list of cardiac lesions for which *completely corrective surgery* is available

MITRAL REGURGITATION

The advent of cardiac bypass techniques also has completely changed the outlook for patients with advancing disability due to this lesion Definitive surgical correction of the regurgitant leak by one of the methods described[39, 53, 54] appears feasible even in advanced states of clinical disability

Pathologic Physiology

Mitral insufficiency results from varying combinations of two primary factors an absolute loss of valve substance from cicatricial retraction and shrinkage of leaflet tissue or chordae tendineae or both and dilatation of the annulus fibrosus

It is of interest that 66 per cent of the patients with significant or severe mitral leaks operated upon to date had a normal sized annulus so that annular plication or circumferential constriction would only have produced stenosis in these cases without correcting the insufficiency In short the corrective procedure must be adapted to the pathology actually found and only the open operation permits this precise type of approach

Open Surgical Procedures

Two new operative technics have been developed for correction of insufficiency The mitral valve is visualized by means of incision in the left atrium approached through a right sided thoracotomy If there is any element of annular dilatation this is corrected by annuloplasty (shortening of the annulus by plication stitches) (Figure 15) If there is a significant loss of valve substance a prosthesis or even a prosthetic leaflet of plastic has been inserted by direct suture[39] Occasionally both techniques are combined to achieve a complete correction

Results

These procedures in varying combinations have proved to be very effective All the pa*tients operated upon to date have had ad*vanced clinical disability (Classes 3 and 4 of the American Heart Association Classification) Yet the operative risk has been low *(10 to 15 per cent) and in the two years since* the first patients were operated upon the

follow up results have been equally promising Not only have the initial gains been sustained but also improvement has continued in some patients long after the operative procedure

The valvuloplasty procedures have been sufficiently effective in some patients with severe regurgitation that postoperatively they have had no detectable murmurs and a normal phonocardiogram over the cardiac apex

This direct vision surgery upon the mitral valve for stenosis has been a very satisfactory procedure, and there is little doubt that the indications for an open operation are likely to be progressively widened in the future as experience with the procedure grows and the backlog of patients with more urgent problems requiring use of the pump oxygenator diminishes somewhat

MITRAL STENOSIS

The patient with pure mitral stenosis in need of surgical relief has a good chance of being benefited by a carefully performed valvotomy by the indirect or blind technics classically described by Bailey Harken and others The principal problems remaining in this field for cardiac surgeons are those observed in the patients with complicating factors that have been found to increase mortality and morbidity while lessening the palliation achieved Although some surgeons have sought to overcome these problems by describing various technical and instrumental variations, the obvious solution seems to us to be a direct vision approach for these patients

The present indications for an open operation for mitral stenosis at this center are listed in Table IX The incisions to approach the valve are the same as those described for regurgitation

TABLE IX

Indications for Open (Bypass Perfusion) Operation for Mitral Stenosis

Indication
Advanced clinical disability
History of embolism
Atrial clots—known or suspected
Restenosis after previous surgery
Mitral regurgitation present or suspected
Multivalvular disease
Children—all

VENTRICULAR ANEURYSMS

The commonest site for ventricular aneurysms encountered has been in the left ventricle subsequent to a coronary thrombosis Others due to traumatic injury to the left or right ventricles have also been treated

Technics for management of these aneurysms without interruption of the circulation have been described, but have been superseded now by use of extracorporeal bypass The open technics have significant advantages in allowing a more complete correction with greater safety to the patient by lessening the hazards of hemorrhage, embolism, cardiac arrest and facilitating the correction of the more complicated types of pathology

ANEURYSM OF THE THORACIC AORTA

Excisional therapy with replacement by a preserved or synthetic graft where necessary has been recognized as the treatment of choice for aneurysms of the aorta However, prior to the advent of methods for cardiopulmonary bypass it had not been possible to treat certain aneurysms of the ascending aorta or aortic arch by this means Now, through the use of bypass methods, it is possible to treat by resection aneurysms located anywhere in the aorta from the sinuses of Valsalva distally to its termination The oldest (and successful) case in this series was in a man 66 years of age

SUMMARY AND CONCLUSIONS

A wide variety of progressively disabling cardiac lesions both congenital and acquired in origin, and in many instances previously inoperable, have been treated surgically among the patients submitted to open cardiotomy utilizing extracorporeal circulation

Although both the knowledge of and the techniques for total body perfusion in man had to be developed and despite the fact that a number of new surgical procedures had to be devised and tested in patients often critically ill with previously hopeless conditions,

the risks have not been at all discouraging when examined in terms of increased human happiness and longevity

In these patients ranging in age from 6 weeks to 66 years the great majority have survived, and most of them are completely cured thanks to the accuracy and scope that visual methods give to surgical technique Moreover, a study of failures early and late leads to a realization that the increased knowledge thereby derived will assist in preventing similar types of failures in the future

Since the time that the detailed analysis of the results in these first 305 patients to have intracardiac surgical procedures by means of extracorporeal circulation was prepared almost 400 additional patients have had open heart procedures utilizing the pump oxygenator This additionally accruing experience has served to confirm and widen the concepts, advanced herein emphasizing the very real benefits of direct vision operations to those patients with the many types of cardiac disease requiring this help

Therefore it may be predicted that open heart surgery is an endeavor likely to continue to grow rapidly and steadily in stature

Beyond these obvious surgical applications the use of a pump oxygenator in the treatment of otherwise irreversible severe shock from trauma, blood loss burns etc for toxemias of various types extensive pulmonary disease or edema and to rest the heart in severe infractions or decompensated states remains virtually an unexplored promise In some of these situations quite likely an artificial heart lung kidney could be lifesaving

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CHAPTER 47

Surgery of the Heart and Great Vessels: Conditions *Not* Requiring Cardio-pulmonary By-pass Techniques

RICHARD L. VARCO, M.D. AND C. WALTON LILLEHEI, M.D.

I PATENT DUCTUS ARTERIOSUS

THIS lesion was the first of the congenital cardiovascular malformations to be successfully operated upon (1938). The procedure of division and suture of the patent ductus as it is almost uniformly practiced today is as nearly a perfect procedure as any in the gamut of surgery since the patient after recovery is restored to a normal physiological state. In addition the confidence and enthusiasm engendered among pediatricians, cardiologists and internists by this demonstrated ability to cope with an imperfection of nature has undoubtedly served to catalyze a steady growth of knowledge and interest in the surgical management of cardiovascular problems. These consequences stand as a classic example of stimulating accomplishment largely brought about through Robert Gross' intrepid leadership.

The historical aspects, physical findings, roentgen manifestations and other specialized diagnostic techniques have all been considered in some detail in an earlier section. In brief, a strongly presumptive diagnosis of patent ductus arteriosus can usually be made with the stethoscope, blood pressure manometer, cardiac fluoroscopy and an electrocardiogram (for exclusion purposes). Although the defect must be differentiated from an aortico pulmonary window, a ruptured sinus of Valsalva, a coronary artery pulmonary artery fistula and certain other rare lesions, the infrequency of these anomalies together with the extremely low risk involved in exploring the ductal area tend to weigh the presumptive clinical diagnosis in favor of a ductus Botalli shunt.

At the present time essentially three problems exist in the surgical management of the individual with a patent ductus: (1) the identification of a patent ductus and the decision to operate upon such a lesion during infancy, (2) the decision whether to ligate or to divide and suture this vessel as the treatment of choice, (3) the management of individuals with severe pulmonary hypertension, in particular those with reversing and reversed ductal shunts.

(1) It is commonly recognized that the diagnosis of a patent ductus in a child during the first few months of life can be difficult. Often the murmurs are not of the "continuous" or machinery like variety. Until the infant loses the pulmonary arteriolar changes (and resistance) present during the fetal period there is a discontinuous quality to the murmur or perhaps only a systolic component. These children, however, can become trying medical problems from recidivous heart failure or recurrent lower respiratory tract infections. These bouts of pneumonia and decompensation can be fatal. Unquestionably in infants found at autopsy to have both pneumonic consolidations and a widely patulous ductus the former is erroneously construed to be the primary cause of death. Other babies with a large patent ductus may suffer from inanition

When a large quantity of blood is leaking into the pulmonary circuit to be ineffectually recirculated, then a failure to gain weight at a normal rate is often a part of the clinical picture. Despite the absence of a typical murmur, this lesion can be suspected, its presence can be confirmed by the use of retrograde aortography. Then after the infant has been prepared as well as possible, and is temporarily free of pulmonary infection, a division of the patent ductus arteriosus in such a case will invariably prove life saving. The vessel encountered in these instances is uniformly as large as the adjacent aorta, and seems to represent almost a continuation of this structure directly into the left pulmonary artery. With competent preoperative management of the cardiac and pulmonary statuses, these children regularly recover from the surgical procedure unless the flow through the ductus is already reversed. The principal challenge under these circumstances rests on the shoulders of the diagnostician. He must be alert to the possible existence of this malformation despite the absence of the usual diagnostic criteria, or another life may be forfeited.

(2) The second problem concerns the choice of either ligating the patent ductus in continuity, or dividing and then suturing this structure. Enthusiastic proponents persist for each course of action. The principal point raised in favor of the former method is that this technique is alleged to be "safer." Critical evidence in support of that conclusion is difficult to obtain. The operative mortality in the hands of those favoring division, and having a large experience with this technique, is quite as low as that achieved by those individuals endorsing in continuity ligation or suture-ligation. Furthermore, the very ductus which is most easily ligated is most easily divided, and that which is most likely to prove difficult of management by the ligature is equally certain to present a problem to those who favor the idea of routine division. In which event, the surgeon having a greater experience and familiarity with the techniques of division and suturing, acquired while treating the easier cases, is certain to have an advantage over the man who ligates all but the difficult ones. There remain two issues favoring division. First, the likelihood of recannalization after such a procedure is virtually abolished, whereas after ligation alone this serious complication has been encountered in approximately 10% of the cases. Too, the early or delayed development of bacterial endarteritis at this site has also been reported and is a disturbing complication of the suture-ligation method. Second, approximately one third of the patients after a ductus operation have a persistent systolic murmur. Inevitably this arouses lingering doubt in the minds of all individuals responsible for the management of this kind of case. Was the ductus completely tied off? This uncertainty can, of course, be banished from one's thoughts after a division. In summary, therefore, the evidence appears to favor, both from an historical and from practical considerations, the routine management of patent ductus by division and closure rather than ligation alone.

(3) The last and most difficult problem to deal with in the surgery of a patent ductus relates to the selection and management of individuals with advanced stages of hypertension induced by the presence of this abnormal shunt. Too, there can no longer be any reasonable doubt that a patent ductus arteriosus is at times provocative of a steadily worsening state of pulmonary arteriolar sclerosis. For some individuals this development can progress rapidly, and even within the first few months of life lead to a reversed shunt. In others, this end stage is reached only with adulthood. In all circumstances, the recognition of this stage in the natural history of that malformation is critical to the soundest management of the individual problem. With rare exceptions the division of a patent ductus in a patient who does not have a continuous murmur, and who regularly shows desaturation at rest in the distal aorta as a consequence of the reversed flow, will promptly be followed by a fatal outcome. These people are doomed prematurely just as are those with an Eisenmenger's complex. Based on present knowledge we have no satisfactory way of dealing with this situation. Their pitiful plight is worthy of our increased research efforts. For those who have progressed somewhat less far on this downhill course, and who show evidence of reversing

CHAPTER 47

Surgery of the Heart and Great Vessels: Conditions *Not* Requiring Cardio-pulmonary By-pass Techniques

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I. PATENT DUCTUS ARTERIOSUS

THIS lesion was the first of the congenital cardiovascular malformations to be successfully operated upon (1938). The procedure of division and suture of the patent ductus, as it is almost uniformly practiced today, is as nearly a perfect procedure as any in the gamut of surgery, since the patient after recovery is restored to a normal physiological state. In addition, the confidence and enthusiasm engendered among pediatricians, cardiologists, and internists by this demonstrated ability to cope with an imperfection of nature has undoubtedly served to catalyze a steady growth of knowledge and interest in the surgical management of cardiovascular problems. These consequences stand as a classic example of stimulating accomplishment largely brought about through Robert Gross' intrepid leadership.

The historical aspects, physical findings, roentgen manifestations, and other specialized diagnostic techniques have all been considered in some detail in an earlier section. In brief, a strongly presumptive diagnosis of patent ductus arteriosus can usually be made with the stethoscope, blood pressure manometer, cardiac fluoroscopy, and an electrocardiogram (for exclusion purposes). Although the defect must be differentiated from an aortico-pulmonary window, a ruptured sinus of Valsalva, a coronary artery pulmonary artery fistula, and certain other rare lesions, the infrequency of these anomalies, together with the extremely low risk involved in exploring the ductal area, tend to weigh the presumptive clinical diagnosis in favor of a ductus Botalli shunt.

At the present time, essentially three problems exist in the surgical management of the individual with a patent ductus: (1) the identification of a patent ductus and the decision to operate upon such a lesion during infancy, (2) the decision whether to ligate or to divide and suture this vessel as the treatment of choice, (3) the management of individuals with severe pulmonary hypertension, in particular those with reversing and reversed ductal shunts.

(1) It is commonly recognized that the diagnosis of a patent ductus in a child during the first few months of life can be difficult. Often the murmurs are not of the "continuous" or machinery like variety. Until the infant loses the pulmonary arteriolar changes (and resistance) present during the fetal period there is a discontinuous quality to the murmur, or perhaps only a systolic component. These children, however, can become trying medical problems from recidivous heart failure or recurrent lower respiratory tract infections. These bouts of pneumonia and decompensation can be fatal. Unquestionably, in infants found at autopsy to have both pneumonic consolidations and a widely patulous ductus, the former is erroneously construed to be the primary cause of death. Other babies with a large patent ductus may suffer from inanition

When a large quantity of blood is leaking into the pulmonary circuit to be ineffectually recirculated then a failure to gain weight at a normal rate is often a part of the clinical picture Despite the absence of a typical murmur this lesion can be suspected its presence can be confirmed by the use of retrograde aortography Then after the infant has been prepared as well as possible and is temporarily free of pulmonary infection a division of the patent ductus arteriosus in such a case will invariably prove life saving The vessel encountered in these instances is uniformly as large as the adjacent aorta and seems to represent almost a continuation of this structure directly into the left pulmonary artery With competent preoperative management of the cardiac and pulmonary statuses these children regularly recover from the surgical procedure unless the flow through the ductus is already reversed The principal challenge under these circumstances rests on the shoulders of the diagnostician He must be alert to the possible existence of this malformation despite the absence of the usual diagnostic criteria or another life may be forfeited

(2) The second problem concerns the choice of either ligating the patent ductus in continuity or dividing and then suturing this structure Enthusiastic proponents persist for each course of action The principal point raised in favor of the former method is that this technique is alleged to be safer" Critical evidence in support of that conclusion is d m . . .

ing division First the likelihood of recanalization after such a procedure is virtually abolished whereas after ligation alone this serious complication has been encountered in approximately 10% of the cases Too the early or delayed development of bacterial endarteritis at this site has also been reported and is a disturbing complication of the suture ligation method Second approximately one third of the patients after a ductus operation have a persistent systolic murmur Inevitably this arouses lingering doubt in the minds of all individuals responsible for the management of this kind of case Was the ductus completely tied off? This uncertainty can of course be banished from one's thoughts after a division In summary therefore the evidence appears to favor both from an historical and from practical considerations the routine management of patent ductus by division and closure rather than ligation alone

(3) The last and most difficult problem to deal with in the surgery of a patent ductus relates to the selection and management of individuals with advanced stages of hypertension induced by the presence of this abnormal shunt Too there can no longer be any reasonable doubt that a patent ductus arteriosus is at times provocative of a steadily worsening state of pulmonary arteriolar sclerosis For some individuals this development can progress rapidly and even within the first few *months* of life lead to a reversed shunt In others this and st . . .

quite as low as that achieved by those individuals endorsing in continuity ligation or suture ligation Furthermore the very ductus which is most easily ligated *is most easily* divided and that which is most likely to prove difficult of management by the ligature is equally certain to present *a problem to those* who favor the idea of routine division In which event the surgeon having a *greater* experience and familiarity with the techniques of division and suturing acquired while treating the easier cases is certain to have an advantage over the man who ligates all but the difficult ones There remain two issues favor

critical to the soundest management of the individual problem With rare exceptions the division of a patent ductus in a patient who does not have a continuous murmur and who regularly shows desaturation at rest in the distal aorta as a consequence of the reversed flow will promptly be followed by a fatal outcome These people are doomed prematurely just as are those with in Eisenmenger's com*plex* Based on present knowledge we have no satisfactory way of dealing with this situation Their pitiful plight is worthy of our increased research efforts For those who have progressed somewhat less far on this downhill course and who show evidence of reversing

(right to left shunt) upon exercise as evidenced by some cyanosis of the toes in contrast to the fingers hope remains for interrupting the progress of the disease before it reaches the above-mentioned end stage of continuous reversal * At the time of an operation to divide this ductus the tenseness and limited length of that communication can prove both disconcerting and treacherous The gradual administration by the anesthetist at this time of a short acting ganglion blocking agent (Arfonad) to reduce somewhat the systemic pressure and hence that in the ductus during the interval while it is under manipulation will materially facilitate and safeguard the subsequent technical steps leading to its being divided and sutured Temporary clamping of the ductus before the individual is committed by its division is also essential At this time if there is an additional fall in systemic pressure and a rise in the pulmonary artery pressure either as estimated by palpation or preferably by direct measurement it can be predicted that this individual is unlikely to tolerate ductal closure On the other hand if the pulmonary artery pressure lessens and no untoward effects on the systemic pressure are measurable the individual is a favorable candidate for division and closure of his ductus despite the presence of a reversal of flow on exercise The outlook is particularly favorable for small children with a potential for enlarging the pulmonary bed during their remaining growth This additional capacity in the pulmonary vascular compartment acquired during the succeeding years when the area is no longer traumatized by systolic impulses of systemic arterial origin will gradually lead to a more normal total pulmonary arterial system Under these circumstances a reasonably good possibility exists of salvaging for that youngster a lengthier life span Certainly there is no justification at the present time for classifying as inoperable the individual with pulmonary hypertension secondary to a patent ductus and in particular any person who still has both a diastolic and systolic phase to the murmur and in whom there is no evidence of a reversal of flow

Individuals with bacterial endarteritis whether developing on or around the ductal site or one of the cardiac valves as a consequence of cardiac overloading by this major leak represent clear-cut indications for operative closure The preferred method consists of treating the bacterial infection with the most effective antibiotic to which the organisms are sensitive Control once achieved should be maintained while healing occurs and for a minimum of 4 to 6 weeks At the end of that time the ductus should be divided If the infection proves refractory to all other forms of therapy and despite a recognition that the surgical risk is materially enhanced in such an instance the ductus should be interrupted in order to cure this patient Otherwise the bacteremia is certain to be lethal

Whereas a normal life expectancy is possible in an individual with a patent ductus the likelihood is that it will be shortened substantially Therefore since at the present time the surgical risk to a person with an uncomplicated ductus is but a fraction of one per cent little justification remains for advising against this curative type of cardiovascular surgery Whether the patient is but a few years old or well past middle age the operation should not prove difficult in the absence of one of the above cited complicating factors Widespread experience acquired during recent years in the management of arteriosclerotic aneurysms and other disease states in far more elderly patients and with advanced damage to the entire vessel wall confirms the fact that the lengthening years of life offer little interference to the healing powers of a sutured vessel At the other extreme young children are particularly tolerant of this operation In all elective cases it can safely and conveniently be done just before the child begins school To operate then is certainly the most effective means of avoiding those preventable sequelae of bacterial endarteritis cardiac decompensation or pulmonary hypertension leading ultimately to reversal of flow Earlier diagnoses and operations on asymptomatic youngsters will largely preclude these complications

* By definition these latter persons would have little or no left to right shunt at any phase of the cardiac cycle

II COARCTATION OF THE AORTA

The importance of identifying this congenital vascular malformation assumed increased proportions with the almost simultaneous reports by Gross and Crawford of its successful surgical management. As a consequence in all individuals suffering from hypertension and in particular those so afflicted during childhood and early adolescence the presence of coarctation must be excluded before other and less favorable mechanisms are indicted. In the relatively few years since the development of this operation thousands of persons have been relieved of their life-shortening hypertension by the surgical removal of this vascular anomaly.

The most common site of coarctation is just distal to the take off of the left subclavian artery. Usually a relatively short segment of the aorta is sharply constricted at about the level of the obliterated ductus Botalli. This area of narrowing is occasionally tapered and hence occupies a longer segment. In other instances the coarctation progresses to a state of atresia. Whereas the most common location is as abovementioned aortic narrowing hypoplasia or even an absence of this vessel can occur anywhere from its beginning to the terminal portion. However severe narrowing in an area proximal to the carotids is uniformly incompatible with any significant interval of life after birth. The term "infantile type" has been applied to areas of coarctation involving the aorta proximal to the carotid vessels. Unfortunately it is a term which also has been applied to those types of coarctation in which the aorta gradually tapers down over a distance of several centimeters to its maximal site of narrowing. Finally it has been identified with cases in which a patent ductus opens distal to the coarctation. The term therefore is virtually meaningless and could profitably be discarded.

At times also coarctation is associated with a patent ductus communicating with the aorta proximal to the area of narrowing. Whenever a patent ductus is associated with a coarctation the technical aspects of the surgical problem are somewhat greater. More important however is the consequence of a ductal communication with the aorta distal to the coarctation. These patients usually have pulmonary hypertension and often it is severe. A reversal of flow i.e. from the pulmonary artery to the aorta and hence factual proof of the severe pulmonary resistance (advanced pulmonary arteriosclerotic changes) can be noted even in relatively young children upon occasion. The direct closure of this patent ductus (with reversed flow) in the absence of a decompressing vent such as a ventricular septal defect is likely to prove fatal either during the operation or shortly thereafter.

The life expectancy of an individual with coarctation of the aorta is approximately two thirds that of his normal contemporaries of the same age. These persons die prematurely from heart failure, bacterial endocarditis (or endarteritis), rupture of an aneurysm at the site of coarctation, a cerebrovascular accident or from heart failure. The vast majority of such premature deaths appear directly related to the presence of the coarctation. It seems reasonable to presume therefore that the establishment of a normal anatomical situation would do much to alter favorably the mortality rate in this group. It is too early to be able to predict with complete accuracy the enhancement in life expectancy which has been achieved in persons successfully operated upon. Nevertheless since the vast majority are either completely relieved of their hypertension or restored to a near normal blood pressure it is likely that their gains are both real and substantial. In some persons the systemic hypertension either persists or recurs after surgery despite the establishment of an adequate lumen at the site of the previous narrowing. This may be related to renal changes which are irreversible despite correction of the aortic lesion. Perhaps earlier operations would avoid these unalterable renal changes.

The diagnosis of coarctation is readily made in virtually all instances on the basis of the physical findings of an elevated systolic blood pressure in the upper extremity as contrasted with the lower portion of the body. The presence of dampened or absent femoral pul

sations (or a comparison of simultaneously secured direct pressure measurements from the upper and lower extremities) its effective confirmatory evidence Tortuous pulsatile intercostal and other accessory collateral vessels in the upper trunk as well as the electrocardiogram and the chest x ray (with rib erosion) can as well confirm this diagnosis At times in very young infants blood pressure measurements made on the extremities are insufficiently precise to permit the categorical diagnosis of coarctation Here the use of retrograde aortography is distinctly advantageous Customarily at this age the procedure is well tolerated Furthermore the identification of this lesion in a child suffering from heart failure of heretofore unknown cause can certainly be a critical consideration in the management of the case

Differences of opinion exist about three aspects of the surgical management of coarctation First there are those who insist that all instances of coarctation during infancy can be more safely managed by nonoperative (medical) means than by recourse to surgery This group contends that these individuals invariably can be tided over one or more bouts of congestive heart failure without incurring a serious mortality rate Arguments continue pro and con about the evidence for this assertion Irrefutable proof showing that either the so-called conservative or the more aggressive operative management is undeniable superior is not at hand Contrary to the opinion of those most vigorously endorsing the non surgical treatment for all infants with coarctation of the aorta is the fact that after one episode of failure in such a child and despite the closest possible attention to the details of medical management a considerable mortality does exist for this group With that complication it probably approximates 10–15% For those individuals with coarctation and associated but curable cardiovascular lesions the eventual mortality from cardiac causes is even higher This is, of course true whether as a group they are all operated upon or treated only by medical means In support of the proposal that surgery can salvage individuals who would otherwise be lost through continued medical management is the fact that medical failures" can frequently be saved by a well done operation Actually the results when working with these more seriously ill patients are as favorable as for the series requiring only medical treatment Furthermore from our limited experience with small children having two or more cardiovascular lesions, including coarctation and these children are often in dire need of treatment because of recurrent bouts of heart failure although the operative mortality has been higher than we wish nevertheless it remains lower than when only medical management was employed under comparable circumstances Finally the outlook among those surviving surgery carried out during infancy is predictably better than those tided over by medical means The latter must undergo ultimately the risk of an operation The argument has been advanced that an anastomosis constructed in a tiny child will be of inadequate diameter during adult life Hence a secondary coarctation operation will be required Although this may be true absolute proof is yet unavailable Furthermore it is usually possible to make an aortic anastomosis in an infant so that the narrowest diameter is far greater than that found in the vast majority of coarctations encountered and resected during adult life The same hesitancy has been invoked against operating upon children electively until they are well into adolescence This suggestion would appear to have even less merit The aorta of a 5 year old child is more than ample particularly since it is often so ballooned out by the very nature of the coarctation as to preclude the development of a secondary narrowing of serious consequences even when the child has grown to adulthood And in fact a limited amount of growth undoubtedly occurs in the line of union during these latter years Whenever it is possible to operate upon young children the increased pliability and distensibility of the blood vessels permit the surgeon to bridge gaps after resection of the coarcted segment which would be both more difficult and certainly under a greater strain or perhaps impossible (without a graft) if attempted during the latter years of early adulthood For these reasons as well as to eliminate the unnecessary hazard of permitting the coarctation to exist

for several years after its identification there is much to recommend surgical correction in the immediately pre school age period and as an elective operation

Debate also continues about the propriety of operating for removal of a coarcted segment in an individual of middle age The argument that these vessels do not heal properly is demonstrably invalid The widespread experience of many surgeons with aortic resections for occlusive arteriosclerosis and aneurysm formation among elderly persons and with far advanced arterial disease reveal that these vessels will uniformly heal safely to themselves or to an inert graft. Too a response in blood pressure after removal of the narrowed segment is usually toward a normal value despite middle age and often the pressure decline reaches an acceptable level The strain thereafter on the cardiovascular system must certainly be reduced

Yet another consideration remains in this discussion of surgery for coarctation It concerns the item of grafts The use of a prosthesis has much to recommend it by permitting the placement of suture lines which are under substantially less distraction strain At times it may be the only means of bridging the gap at hand after excision of the involved area Nevertheless the long term fate of these substitutes remains in doubt. Good agreement has not even been reached as to which is the "best graft Certain unfavorable changes have occurred in some which have been in place merely a few years The possibilities are great and disturbing that additional graft deterioration will occur with time When it is possible therefore to operate for coarctation upon a young child it is less likely because of the increased vascular stretchability that this individual will need a grafting procedure The patient so managed thus retains the birthright of his own vessel throughout his future

A disturbing complication following an otherwise satisfactory resection for coarctation is infrequently encountered Relatively early in the postoperative convalescence the patient will complain of abdominal pains exhibit fever, manifest some ileus and in the more severe cases this will progress to the stage where an abdominal operation is indicated At the time of exploration diffuse areas of localized necrosis and inflammatory reaction are encountered The microscopic picture is that described for periarteritis nodosa The process can be so serious as to require resection of varying lengths of the bowel Despite recourse to this maneuver some have progressed or exhibited such widespread involvement that death has eventuated The exact mechanism involved in the genesis of this complication remains uncertain It appears likely that the abrupt imposition of high systolic peaks (and perhaps low diastolic depths) through the arterial tree below the coarcted segment induces intolerable consequences to the vascular ramifications supplying the intestines The greater concentration of bacteria and bacterial products in this region may well be more than coincidental in the development of these areas of necrosis Recently certain cases which appear to be typical of this syndrome have been successfully managed by the administration of intestinal antibiotics long acting sympatholitic drugs and cortisone

In conclusion it can be stated that the diagnosis of coarctation is usually made readily once it has been suspected and it should be thought of in any case of hypertension in a young person The physical findings the x ray picture and if necessary aortography are ample means to arrive at the diagnosis Once the lesion has been identified surgery is indicated A child with coarctation who develops heart failure is in jeopardy The risk is magnified considerably if there are associated cardiovascular lesions To insist uncompromisingly on medical (non operative) management for all of these individuals is unlikely to save as many as the combined use of medicine and surgery relying on the latter when the child fails to rally and sustain these gains achieved under the best form of medical treatment If serious complications do not supervene the operation can safely be postponed until the pre-school age or slightly later However to procrastinate many additional years would appear to be more disadvantageous than worthwhile It seems clear as well that surgery for coarctation in the middle-aged

person is neither technically impossible nor physiologically unsound. Finally the end results of grafting techniques for coarctation and the development of serious or fatal episodes of vasculitis remained the unsolved problems in the management of this malformation.

III MALFORMATIONS OF VASCULAR ORIGIN WITH ABNORMAL COMPRESSION OF THE TRACHEA AND/OR ESOPHAGUS

Certain embryological anomalies of the aortic arch and its primary ramifications provoke to varying degrees narrowing of the trachea and/or esophagus. Whereas at times the intrusion is inconsequential, upon occasion the involvement can jeopardize life, and this is invariably during infancy. Nevertheless, serious as this amount of narrowing can be, it is usually possible to relieve it by appropriate surgical measures. And again a crucial phase of the problem is the diagnosis.

The two most frequent forms of serious tracheal and esophageal compression are some variant of a double aortic arch or the insertion of a ligamentum arteriosum into a right descending aorta. Each forms a "ring" about these structures. The relative lack of stretch in the involved vascular and fibrous components prevents a proportionate growth in the encircling "ring." As a consequence normal respiration and alimentation are interfered with. Typically the child suffers from recurrent respiratory infections and may repeatedly contract pneumonia. The baby exhibits inspiratory difficulty which is characterized by a wheezing and stridor that appear to be partially *relieved* when the child assumes an hyperextended position. On the contrary manual attempts to straighten the child out and in particular with forward flexion of the head and neck are followed by evidence of pronounced respiratory obstruction. The ingestion of liquids may precipitate or exaggerate the breathing problem. Upon these occasions the child was incapable of forcing this material through the narrowed area and as a consequence some spilled over into the larynx and down the trachea. The persistence of this obstructed state for any *length* of time is almost certain to damage the lungs and even destroy the *infant*.

Identification of the general *type* of lesion is usually quite readily made once its existence has been suspected. By means of films taken in the postero anterior projection and lateral positions and, as well, whenever necessary in combination with the instillation of water soluble radiopaque material into the esophagus or trachea, the sites and extent of the narrowing can be visualized. Usually bronchoscopy and esophagoscopy are unnecessary and unlikely to contribute any significant additional information.

The frequent association of respiratory complications often culminating in pneumonia demand the best possible preoperative preparation in order to avoid this or related serious complications in the postoperative period. Proper positioning of the child will minimize these difficulties from respiratory and esophageal obstruction. Also painstaking assistance during each feeding period will reduce the hazard of aspiration and its grave consequences. At times gavaging the infant may be necessary in order to by pass the *constricted* segment of the compressed esophagus. Whenever feasible the pulmonary status should be treated until residual infection has been eliminated. The use of antibiotics appropriate to the specific pathogen involved is certainly in order.

The *surgical management* of these lesions requires a precise dissection of the vascular ramifications of the aorta. Once these have been accurately identified, the lesser vessels completing the ring about the trachea and esophagus are *simply* divided and closed by ligature or a running suture of fine silk. That the carotid vessels continue to receive an uncompromised flow is a critical issue in each case. *Any* accessory vascular attachments which encroach on the tracheal or esophageal lumina must be totally freed at this *time*. In general, once the trachea and esophagus have been carefully unlocked from this limiting ring they assume their normal unrestricted position in the mediastinum. Those instances where these structures have been encircled and abnormally narrowed by an obliterated ductus Botalli (attached to a right descending aorta)

are even simpler to free since there is less cause for concern about hemostasis after division of this band However, inasmuch as the precise level of its obliteration is uncertain it is well in each case to secure the severed ends by a stick tie type of ligature Exposure to this whole area for the double aortic arch and the other "rings is satisfactorily accomplished by an anterior incision in the third left interspace (or the bed of that rib) plus division of the adjoining cartilages or (more simply in these infants) by a vertical extension of the intercostal incision as a full thickness median sternotomy The thymus can then be reflected or excised as appears indicated Opening the pericardium and beginning the dissection at that level often provides for an earlier orientation of the problem at hand in that particular case

Postoperatively these children can exhibit annoying and threatening accumulations of tracheal mucus An adjunct for managing this consists of repeated gentle suctioning for both the pharyngeal accumulations and the tracheo bronchial phlegm, whenever the latter is audible to auscultation In addition cold moist air humidifiers and nebulizers for antibiotics and detergents assist in freeing the tenacious grasp of this excess mucus Postural changes and a rocking bed are also handy adjuvants for combatting these accumulations in the early postoperative convalescence Once the child has been tided over this period recovery is usually prompt and predictable The obstruction to alimentation having been relieved at operation this rarely causes any trouble during the convalescent interval

Occasionally other vessels i e anomalous origin and course of an innominate artery or the oblique path of a right subclavian artery arising from the left descending aorta can intrude on the trachea or esophagus respectively The latter vascular anomaly occurs far more frequently in children with congenital heart disease than the incidence of cases with any significant and demonstrable obstruction to the gullet

IV PULMONARY OUTFLOW TRACT OBSTRUCTION WITH AN INTACT VENTRICULAR SEPTUM

Outflow tract obstruction in this group of cases is due either to stenosis of the valve of the infundibulum or of both Far and away the greatest number have involvement of the valve although in many because of the secondary hypertrophy associated with an increased work load on the right ventricle there is an encroachment by enlarged trabecular fibers and an oversized crista supraventricularis into the outflow channel of the right ventricle

For some time legitimate differences in viewpoint have existed in the minds of surgeons dealing with this problem Whether wisdom dictates an operation to correct these lesions under direct vision or to attempt to restore a more normal opening by indirect approaches (Brock) remains an incompletely answered problem However sound argument cannot be made in favor of direct vision surgery which is limited to an operation on the valve and is carried out through an opening in the pulmonary artery (as under hypothermia) Since no relief to any outflow tract obstruction in the subvalvar area has been added to that operation the closed (transventricular) operation of Brock is probably as good and also more safe Revision of the outflow tract through a ventriculotomy unquestionably provides the most satisfactory visualization of the pathological anatomy and hence permits the most precise type of plastic repair Nevertheless despite this generous access to the areas of involvement the uniform and immediate elimination of considerable postoperative gradient between the right ventricle and the pulmonary artery is difficult to bring about Moreover the additional complexities inherent in cardiopulmonary by pass techniques still loom as a serious deterent to the routine use of such methods to the exclusion of all others With greater experience in the use of extracorporeal circulation this method is likely to find an ever wider application and ac-

ceptance as the treatment of choice for outflow tract obstruction involving the valvar region. Whenever there is infundibular pulmonic obstruction, excision of the fibromuscular ledges intruding into the outflow tract under direct vision utilizing cardiopulmonary by-pass is the only practical method of treatment. Yet another advantage accruing from the application of open heart methods to all cases is the finding from time to time of a ventricular septal defect which had been quite unsuspected on the basis of clinical findings or catheterization data. Once the outflow tract obstruction in the right ventricle has been released, such an opening carries a lethal potential if it is not closed during the same operation. Otherwise it can impose an abrupt and intolerable left to right shunt on the heart in the postoperative interval. In fact, although isolated infundibular obstruction with an intact ventricular septum does occur, it is so uncommon that when diagnosed the probabilities are almost as great that the individual has a ventricular septal defect, often with virtually balanced pressures within the ventricles, which consequently has remained undetected. For this reason, those individuals with infundibular obstruction alone or in combination with valvar obstruction who require surgical relief are best managed by open heart methods which incorporate the use of cardiopulmonary by-pass arrangements that permit an extended surgical procedure within the chambers of the right heart.

More commonly, an individual with outflow tract obstruction and an intact ventricular septum suffers from valvar stenosis. The symptoms, signs, physical findings, electrocardiographic data, and roentgen appearance have all been considered in an earlier section. In general, these individuals are readily diagnosed, particularly if they remain acyanotic. In fact, given this clue, the diagnosis can be firmly offered in many instances from a simple posteroanterior roentgenogram of the chest. Pulmonary valvar stenosis is a strong possibility in an acyanotic person with a systolic murmur and thrill along the left sternal border and a cardiac silhouette which definitely includes evidence of post-stenotic dilatation with asymmetrically sized pulmonary arteries together with an enlarged right auricle, right ventricular hypertrophy, and decreased or normal vascularity in the peripheral lung fields. The clinical problem is somewhat less easily analyzable when the outflow tract obstruction is associated with an auricular septal defect large enough to permit a significant right to left shunt and hence the appearance of peripheral desaturation. Sharply defined angiocardiographic silhouettes are of real value along with selective angiocardiography for resolving correctly this differential diagnostic problem as to whether a pentalogy of Fallot may exist. Right ventricular pressure tracings are worthwhile also, for if the tension in that chamber substantially exceeds the simultaneously measured systemic value, a ventricular septal defect can be ruled out.

Once the correct diagnosis has been established, a major problem still remains. Which patients should be operated upon? Certainly all individuals with any progression in their symptoms evoked by this congenital malformation (those exhibiting heart failure, those with progressive degrees of cyanosis or a rising hematocrit, and those with right ventricular hypertension beyond 60 to 70 mm. Hg when the individual is essentially at basal or resting conditions) are worthy candidates for surgical relief. The major reservations about recommending an operation arise in the case of individuals whose right ventricular pressure is no more than 60 to 70 mm. Hg and, in particular, if that person has already reached adulthood and hence presumably is not likely to increase the cardiac work load much thereafter. To be sure, a more realistic determination of the strain to which the right heart is being exposed can only be secured when these values are obtained while the individual is exercising moderately. Likewise to be considered separately is a pressure of 70 mm. Hg in a toddler. This value is almost certain to increase steadily as the demands for a far greater pulmonary flow are made with time and body growth. Occasionally a patient with pulmonary outflow obstruction exhibits cyanosis due to a right to left shunt at the atrial level and on catheterization reveals only moderate deviation of the right ventricular systolic pressure. Since right ventricular decompensa

tion is a necessary precursor to a right to left shunt at the atrial level, this type of case can have a more severe stenosis than is revealed by the height of his pressure tracing Confirmation of the existence of his problem and of the right ventricular failure is found rather in the measurement of the right ventricular end diastolic pressure This will be elevated and indicates heart failure Therefore as a group these persons are also in need of surgical correction of their defects The safest and most certain means for curing both the outflow tract obstruction and closing the atrial septal defect is through the use of direct vision open heart surgery with a cardio-pulmonary by pass The need to individualize all cases should be well recognized by cardiologist and surgeon alike Whenever it is reasonably safe to defer the operation to an elective interval there are technical advantages in taking this postponement into the grade school period While this applies both to the use of closed methods and the direct vision correction it is probably more significantly applicable to the former

The original Brock Sellors technique of closed pulmonary valvotomy is technically not complicated can be made to yield satisfactory results in the hands of an individual experienced in its use and need concede no addition in principle from the various and numerous modifications which have subsequently been introduced In essence appropriately sized knives with cutting edges along the diamond shaped configuration are passed through the musculature of the right ventricle down the outflow tract and then forced through the orifice of the narrowed pulmonary valve in order to bifurcate it Subsequently dilating mechanisms passing through the same hole in the ventricular musculature insure the enlargement of the valvar orifice to the utmost tolerance of the pulmonary artery The blood loss for these steps need hardly exceed a few ounces The quality of the thrill in the pulmonary artery promptly changes after a satisfactory division and dilatation Usually no serious question arises about the valvar obstruction having been relieved Additional confirmation of this fact can often be obtained by the operator inserting his finger through the ventriculostomy opening and then projecting it backward into the right ventricular chamber and then forward down the pulmonary artery without encountering more than the functional obstruction previously alluded to Recovery from this operation is usually prompt and without significant complications With attention to elimination of those cases carrying an organic infundibular obstruction the results are good albeit rather less perfect than is attainable in the management of the patent ductus arteriosus or coarctation of the aorta With attention to the item of the selection cited above the closed method has much to recommend it at this stage of our technical advancement

V OTHER ANOMALIES WITH AN INADEQUATE PULMONARY FLOW

The development of direct vision intracardiac surgical techniques has substantially altered the management of the tetralogy of Fallot malformation formerly treated by a shunt procedure The palliative anastomotic operations of Blalock and Potts which were the principal means of benefiting the individual crippled by the defects present in Fallot s tetralogy have been replaced in this clinic by curative operations carried out by open heart surgery utilizing a cardiopulmonary by pass arrangement. The immediate risk to these patients has been higher However in considering this matter it should be recognized that not only is the mortality of the open operation decreasing steadily with increasing experience but the cumulative mortality (immediate and late) for the shunt operations appears to be greater than that which it is reasonable to anticipate will apply for curative procedures The reasons for the continuing attrition among those tetralogy cases treated by a shunt operation are threefold the small child recovering from a shunt operation designed to relieve the insufficient pulmonary flow associated with a Fallot s tetralogy is quite likely to outgrow this palliative contribution He thus becomes ever more crippled by this limitation and although

his demise has been postponed for a few years, nevertheless he does succumb prematurely from pulmonary decompensation a rising hematocrit, and vascular thromboses or other consequences of chronic anoxia Secondly although his life has been prolonged no increased protection has been provided this individual against death from bacterial endarteritis adjacent to the shunt or from brain abscess to which he is particularly vulnerable because of the septal defect Finally if the shunt is disproportionate and larger than the cardiac reserve can tolerate (a status more likely to occur in aortico-pulmonary anastomoses) recurrent bouts of chronic failure can supervene When the patient survives but because of progressive inadequacy in the shunt currently requires an open heart procedure that operation is severely complicated by technical problems arising from the earlier palliative procedure Because of these considerations as well as from poignant experiences with the problems of hemostasis in an individual who has been heparinized and then must have these vascularized adhesions (which became established after a previous shunt operation) taken down in order to disconnect this leak as a preliminary to a by pass operation we have come to endorse the belief that elective anastomotic operations for tetralogy of Fallot patients are very undesirable The roles of the shunt operation at this time appear to be two a life prolonging technique for gravely ill children with Fallot s tetralogy in those areas where curative surgery by direct vision methods are not available and secondly for certain lesions (tricuspid atresia transposition of the great vessels with pulmonary stenosis) in which with present knowledge (despite the use of open heart techniques) the malformation remains incurable Under these circumstances the establishment of a satisfactory systemic artery pulmonary artery shunt can be an effective means of achieving palliation which in some instances is synonymous with a longer life and a more pleasant one albeit with no serious anticipation that a normal life expectancy is likely When ever such a shunt operation is to be carried out the most satisfactory one when technically possible consists in uniting the subclavian artery off of the innominate to the side of the adjacent pulmonary artery End to end systemic pulmonary artery anastomoses should be avoided because of their tendency to provoke proliferative pulmonary arteriolar changes with consequent loss of the effectiveness of the shunt. They also have a greater tendency to thrombose early in the postoperative phase If an end to side union cannot be brought about utilizing a systemic artery at least 3 and preferably 4 or 5 mm in diameter then the direct side to side union of the aortic and pulmonary systems as described by Potts remains the next best choice After satisfactorily completing the anastomosis either by the Blalock or Potts plan a palpable thrill and an audible continuous fistulous type murmur and an evident increase in the oxygen saturation of the arterial blood should be apparent The increased volume now circulating through the lung via the systemic artery pulmonary artery leak raises thereby the patient s exercise tolerance to a more comfortable level

Quite infrequently an infant or young child with Fallot s tetralogy will have extreme hypoplasia or agenesis of the pulmonary artery which can extend well out into the lungs For the former a shunt operation when technically feasible may enlarge the caliber of the vessel due to the factor of an increased flow For the latter no anastomotic procedure is possible and little can be done to augment the pulmonary flow The establishment of an increased number of chest wall collateral communications with the lung by removing the parietal pleura may be of some slight benefit to such a child

VI PARTIAL AND TOTAL ANOMALOUS PULMONARY VENOUS RETURN

The diagnosis of pulmonary venous anomalies has been dealt with in an earlier section For the more complete forms the patients usually need relief by appropriate open heart surgical techniques

It is extremely uncommon for any instance of anomalous venous return to exist without at least a probe patent foramen ovale and more often it is associated with a secundum type of atrial septal defect All instances of total anomalous venous return require the coexistence of an interatrial shunt The operative management of total anomalous insertion of the pulmonary veins is, therefore, one uniformly complicated by the presence of an atrial septal defect Since the ideal management of this lesion can only be achieved by direct vision intracardiac surgery, the management of the partial anomalous venous return, in a certain sense, is a secondary consideration Often it is possible to realign the atrial septum so that the previously abnormal openings thereafter come to lie in the left atrial chamber and where they should have been originally Occasionally an isolated pulmonary vein will empty high and directly into the superior vena cava With cardiopulmonary by-pass techniques a partition may be constructed in the back wall of the cava down which the pulmonary venous return can drain into the left atrium, without provoking pulmonary venous congestion and segmental lung edema An alternative maneuver is to clamp and divide this vein adjacent to the cava, closing the distal end and then anastomose it to the side of a more low-lying pulmonary vein having first occluded, temporarily, the corresponding pulmonary artery so as to minimize parenchymal congestion during the establishment of the new opening

Certain forms of total anomalous pulmonary venous return are associated with an hypoplastic left atrium and mitral valve This is particularly true of those cases where the entire pulmonary venous return from both lungs drains via a common channel into the left innominate vein, the coronary sinus the superior vena cava, or the portal circuit, and in conjunction with which there is a relatively limited opening in the atrial septum Under these circumstances, an excessive recirculation through the pulmonary circuit exists and a restricted flow moves into the left side of the heart The latter chambers are underdeveloped If the entire pulmonary venous return is abruptly directed into the left atrium and the septal defect closed all in one stage great care must be exercised in the management of blood replacement and fluid administration if serious or fatal pulmonary edema is to be avoided

This one stage correction utilizing by-pass techniques appears preferable to us although we acknowledge our limited opportunities to date for managing this lesion An alternative approach is the two stage procedure in which a generous-sized opening is created between the collecting vein from both lungs and the left atrium The establishment of this wide open anastomosis permits a large volume to enter this side of the heart, far more than it customarily receives Any tendency toward an unsuitable elevation in the pulmonary venous pressure is completely prevented, however, by the optional drain off through the distal communication of the anomalous venous limb which remains open also After a suitable interval for adaptation, this and the atrial septal defect can both be closed with the confident expectation that no untoward episodes of pulmonary edema are likely to complicate the convalescence It is to be emphasized, however, that, in general, we believe most instances of total anomalous venous return require direct vision intracardiac surgical techniques, and are best managed by a one stage operation In a sense, cor triatriatum should be considered as a form of anomalous pulmonary venous return, and it too is best dealt with by a plan which permits inspection and orientation as to the exact nature of the lesion and then as long a time as may be required for restoration of a functionally normal circulation

VII. ANOMALOUS ORIGIN OF CORONARY ARTERY

Abnormal origin of a coronary artery probably, on the other hand will not require such elaborate equipment for its reimplantation onto an arterialized vessel Provision for a

trickle of oxygenated blood through this tributary while it is being restored to a more suitable physiological environment should suffice to protect the myocardium momentarily. The chief problem is that of suspecting the presence of this lesion soon enough for these children often die in the first few months after birth.

VIII AORTIC STENOSIS

The diagnostic features of aortic stenosis have been presented. In any particular case the main issue is the need for operative relief by that individual and how much risk and gain are likely to be his. The use of left heart catheterization is certainly important in establishing more accurate criteria for recommending an operation and as well for evaluating the accomplishment. To wait until syncope, angina and recurrent heart failure exist before there is an acknowledged indication for operation is to forfeit the best chance for surgical help. Moreover the appearance of a left ventricular strain pattern in the electrocardiogram is also a late manifestation of this lesion.

Firmly held differences of opinion will probably continue to exist for some time between those advocates of closed methods for managing aortic stenosis and those who endorse the direct vision type of operation. In acquired lesions each may be willing to concede that in many instances with valves irreparably destroyed by accumulations of calcium cholesterol and ulceration only an imperfect outcome is achieved by either method. For congenital aortic stenosis with its pliable leaflets usually free of damaging deposits most all surgeons agree that open surgery is preferable, quite safe and curative. Moreover the experiences gained in the fashioning of precise valve orifices in this relatively restricted area are certain to prove valuable later on when satisfactory prosthetic replacements become available. Truly curative surgery for most all patients with this affliction will then be possible.

IX MITRAL STENOSIS

The individual with mitral stenosis in need of surgical relief has a good chance of being benefited by a well planned and carefully performed commissurotomy on this valve. The principal problems remaining in this field for cardiac surgeons are those of embolization at the time of surgery and those individuals with indeterminate degrees of mitral stenosis and insufficiency and occasionally the person who restenoses his mitral valve after seemingly an adequate freeing of the adherent leaflets. The latter type of problem can usually be managed by a re-operation. Of the other two problems that of uncontrollable embolization at the time of surgery is certainly a very distressing complication. To date methods designed to eliminate this problem have not succeeded (anticoagulation regimens, clamping of the cerebral vessels, flushing of the auricle, etc.). It seems a reasonable prediction that with an increasing familiarity with pump oxygenator systems both that complication and the management of combined mitral lesions (insufficiency and stenosis) will be dealt with through this means. Also when a satisfactory mitral valvar prosthesis is available as a replacement unit the shift to direct vision management of these valvar problems is likely to proceed rapidly.

Meanwhile the standard method of mitral commissurotomy with the finger or an instrument is a modestly effective means of relieving the cardiac burden created by an intolerably narrowed mitral orifice. Thereby considerable protection can regularly be brought to those who have suffered from previous embolic episodes. The likelihood of this complication subsequently developing is materially reduced after the establishment of a widely patulous mitral orifice to replace the narrow former opening.

Recovery from this procedure is usually uneventful. An occasional patient develops tachycardia, restlessness, unexplained fever

and bizarre mental aberrations which though transient can be disturbing These are usually self limited and may in many instances be due to a pericarditis and myocarditis of a traumatic origin rather than a recrudescence of their rheumatic carditis Usually these states need no treatment other than for symptomatic relief They have unfortunately been lumped into that meaningless category of "post commissurotomy syndrome

Occasionally also a patient will develop difficulty because of a prolonged period of sodium restriction imposed as a part of the medical regimen in preparation for the operation An ability to hold water despite its low electrolyte content which occurs in the severely diseased mitral patient at times predisposes him to water intoxication The imprudent intravenous administration of what would otherwise seem to be reasonable volumes of 5% glucose in distilled water in such a case is capable of provoking convulsions The fluid replacement therapy under such circumstances therefore should include electrolytes of a pattern and quantity sufficient to prevent this complication Furthermore if continuous gastro intestinal siphonage is employed provision for restoration of this additional salt loss should be included The convalescent commissurotomy case who receives a substandard volume of fluid the first few days is in no danger from dehydration and usually enjoys a smoother recovery

Most patients with chest wall incisions are inhibited from their normal ventilatory excursion and in particular from coughing both by the local distress in the incision and from the traumatic pleuritis associated with their operation Also the tendency toward retention of tracheo-bronchial secretions is enhanced in the patient with pulmonary congestion Under these circumstances it is important if one is to achieve a smooth convalescence that the patient either cough and raise this material voluntarily or that such accumulations be extracted by periodic use of aspiration equipment inserted through the larynx and down into both sides of the tracheo bronchial tree

As stated above the postoperative mitral stenosis patient is generally a simple problem to manage granted that a satisfactory orifice has been developed at the time of surgery The absence of strain on the left ventricle with this lesion and the minimal trauma imposed on the heart by this operation lend assurance that the usual convalescence from a mitral commissurotomy will be steady and gratifying

In turn those patients suffering from mitral insufficiency are best dealt with by open heart surgery utilizing cardiopulmonary bypass equipment The results after appropriate attention has been given to correction of an excessive circumference in the annulus or the replacement of valvar substance loss by a prosthesis are quite encouraging In fact mitral insufficiency may prove to be a more hopeful lesion to treat than its counterpart stenosis

X CORONARY ARTERIAL INSUFFICIENCY

Surgery for coronary artery disease has long attracted the surgeon's interest as well as those predominantly concerned with experimental approaches to this problem Despite the expenditure of vast amounts of time and money operations with only a limited benefit are as yet available and no curative procedure has been developed for coronary arterial insufficiency To date the main benefits of an operation appear to be the relief of subjective symptoms In this regard the installation of abrasives and irritant materials into the pericardium appears to be as effective as other more complicated procedures A sincere concern with the magnitude of this problem unquestionably motivates the intense amount of attention which it has received in widely separate medical centers throughout the world Nevertheless persons intimately involved with progress in this field remain in a quandary or at least in a state of essential difference of opinion about the relative effectiveness of various methods (both in the research laboratory and clinically) with regard to their capacity to protect against degrees of coronary artery occlusion and to increase longevity Legitimate doubts therefore remain about the clear cut superiority of any one

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of a variety of methods (internal mammary artery implantation coronary sinus and vein arterialization pectoral muscle omental pulmonary intestinal revascularization of the myocardium) Recently it has been suggested that merely ligating the internal mammary arteries distal to those branches supplying the pericardium relieves angina and protects the patient with coronary arterial insufficiency Proof that this is true is likewise unavailable A few attempts at endarterectomy for the segmental areas of coronary arterial obstruction have been reported by Bailey The technical problems related to suturing and anastomosing the diseased vessels are considerable not to mention those associated with diagnostic problems related to the selection of suitable patients These difficulties will require the development of additional specialized techniques if they are to win any widespread adoption At this time it appears more like that manipulating the metabolic responses which create coronary vessel changes in the individual will in the long term prove more successful than even the most heroic approaches attempted to date

XI CONSTRICTIVE PERICARDITIS

Typical cases are rarely overlooked by the alert clinician The presence of a quiet heart paradoxical pulse small pulse pressure elevated venous pressure roentgen evidence of impaired ventricular filling (and in some calcific accretions) are strong evidence that the patient has constrictive pericarditis Further supportive data can be found in the electrocardiogram which shows low voltage for the QRS complexes and flattened to inverted T wave changes in most leads Cardiac catheterization is neither indicated nor necessary for a diagnosis in most cases although in some the right ventricular and atrial tracings are quite typical

The surgical problems are two (1) the propriety of early (even prophylactic) operations in patients with active tuberculous pericarditis When some evidence of beginning tamponade or evident constriction exists even if the patient has an active tuberculosis process this lesion can be approached surgically without undue risk granted that the organisms are known to be sensitive to chemotherapy The high degree of effectiveness of present day antibiotic management virtually assures the individual against systemic spread while under this protection Furthermore the wounds necessary to relieve the constrictive pericarditis though contaminated at the time are unlikely to develop foci of tuberculous involvement

(2) The second area of dispute relates to the extent of the decortication required in cases of constrictive pericarditis A limited operation is deemed quite adequate by some This consists of removing the reactive peel (and pericardium) over that portion of left and right ventricular surfaces which can be exposed with a left-sided thoracotomy Others are convinced that only the "complete" procedure will succeed which frees both vena cava the ventricles including the apex the atrio ventricular groove and the pulmonary veins The latter choice requires a sternal split transverse or vertical to achieve the exposure of these several areas Whereas the latter more extensive procedure has much to recommend it theoretically the extent of the dissection is a heavy burden to impose on the patient already seriously ill with constrictive pericarditis When it is used in children it is usually accepted better than by adults especially among patients well into their later years Conceivably this abrupt release of a large myocardial area from bondage permits it to dilate unduly Unhampered as it then is chronic heart failure persists for weeks in some cases Recovery on the other hand following a less complete removal of these constricting elements has seemed clinically smoother Edema high venous pressure hepatomegaly and ascites slowly but steadily disappear Perhaps this incompletely decorticated heart has thus been protected" against the disadvantages of excessive enlargement by these residual areas of adherent but scarcely constrictive pericardium Furthermore the end result of this plan often

meets the desired preoperative objective re lief of the patient's cardiac problem

Therefore, although multiple sites of restriction to free flow can circumstantially be implicated, the commonest (and probably the essential) region for these constrictive forces to act on is the trapped left ventricle Obstruction here to diastolic filling initiates and promotes the physiologic sequence ultimately recognized clinically as constrictive pericarditis

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CHAPTER 48

Injuries to the Heart and Great Vessels

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BLUNT TRAUMA OF THE HEART

SOME degree of injury to the myocardium occurs in most crushing injuries or contusions of the chest wall. The myocardium because of its extreme vascularity tolerates minor degrees of contusion well; however, more severe contusions produce readily demonstrable clinical symptoms. The absence of external evidence of trauma does not in itself preclude injury to the myocardium, particularly in the individual with a flexible chest wall. As a routine practice an electrocardiographic tracing is taken on all patients with chest wall injuries promptly after the injury has occurred and this tracing is then repeated several days after the injury. The absence of any changes on the electrocardiographic study may be taken as good objective evidence to indicate no myocardial injury and this study may be of great value from the medicolegal standpoint. Progressive electrocardiographic changes may be the only indication the physician has that myocardial damage has taken place.

SIGNS OF CARDIAC CONTUSION

Signs and symptoms of cardiac contusion may appear early or late following injury. We have on several occasions observed patients who developed severe cardiac abnormalities as long as 2 and 3 weeks after the original injury. The following signs strongly indicate injury to the myocardium: (1) Progressive electrocardiographic changes. (2) The appearance of arrhythmia with the exception of extrasystoles. (3) Friction rub. (4) Evidence of cardiac enlargement not present prior to injury. (5) Signs of pericardial tamponade.

BLEEDING AND TAMPONADE FOLLOWING CONTUSION OF THE HEART

The physician must be alert to the possibilities and recognition of tamponade following blunt trauma. The diagnosis is at times complicated by the fact that tamponade may occur late in the picture. Characteristically the patient shows a fall in blood pressure and pulse pressure. The skin is pale and the patient may perspire freely. Distention of the peripheral veins with increase of the venous pressure may be the outstanding clinical sign available for diagnosis. One cannot rely very much on the changes seen on x-ray since the degree of enlargement of the pericardial shadow may be relatively slight and not readily discernible with the available x-rays. Usually the heart tones are muffled and quiet to auscultation; however, it is entirely possible to see a picture of pericardial tamponade in which the heart tones remain rather loud inasmuch as the heart can float anteriorly on a pool of slowly accumulating blood and be compressed against the anterior chest wall.

TREATMENT OF CARDIAC CONTUSION

The treatment of contusion of the heart is similar to the treatment of a patient with acute coronary disease. He is kept at rest and an attempt is made to supply the myocardium with well oxygenated blood at normal pressures. This implies maintaining the patient's blood pressure at normal levels and maintenance of normal hemoglobin and blood volume levels. These patients will frequently have concomitant injuries to the chest wall and lungs and the maintenance of normal oxygen saturation of the peripheral blood must be sustained by proper attention to the treatment of concomitant chest wall and pulmonary injuries. Tamponade which occurs secondary to cardiac contusion can usually be relieved by aspiration of the pericardium. We have seen an occasional case in which thoracotomy was necessary to relieve tamponade since the blood had clotted within the pericardial sac and could not be removed by needle aspiration.

Mortality figures are difficult to ascertain since in the cases in which death occurs there are usually other severe complicating injuries and death is usually ascribed to other factors. Late sequelae to myocardial contusion appear to be uncommon. Constrictive pericarditis has been reported as a late complication of traumatic hemopericardium. Evaluation of symptoms following recovery from the original injury is frequently complicated by the possibility of compensation neurosis and made difficult by the absence of good objective tests to measure minor disturbances in cardiac function.

PENETRATING AND PERFORATING WOUNDS OF THE HEART

In the treatment of penetrating or perforating wounds of the heart it is of considerable importance to determine the type of instrument that has caused the wound and also to accurately ascertain the direction and course that it has pursued. In general two rather distinct clinical pictures may be seen in penetrating and perforating wounds of the heart. First, those whose symptoms are due primarily to tamponade with very little actual loss of blood and secondly, those whose symptoms are due primarily to blood loss with no tamponade effect. There are, of course, others in whom there is both tamponade plus sufficient loss of blood to produce symptoms. In the case of a penetrating wound in which the instrument passed directly into the mediastinum from the anterior surface of the chest and then penetrated the chamber of the heart or intrapericardial vessels without traversing the pleura the actual blood loss is very slight. The blood rapidly accumulates within the pericardium and the picture of pericardial tamponade becomes apparent after a loss of only about 200 ml. of blood. After 400 ml. of blood have become trapped in the pericardium life becomes impossible unless steps are promptly taken to empty the pericardium. Wounds of the atria or the intrapericardial portions of the large vessels may cause rapid death from tamponade unless there is an additional opening in the pericardium which allows the blood to escape into the pleural space whereas wounds of the myocardium may be oblique and the myocardium will bleed only in systole. In the latter case there may be considerable delay in the appearance of tamponade. In contrast to the above type of case in which tamponade is the paramount symptom one sees patients in whom the major factor is shock from blood loss with very little tamponade effect. In this second group the instrument passes through the pleura before entering or perforating the chamber of the heart or the intrapericardial vessels. This results in loss of large amounts of blood into the pleural space with the appearance of the clinical picture of shock. In these patients it is of great importance to distinguish the symptoms of shock from tamponade. An x-ray of the chest will demonstrate the presence of a large hemothorax and will aid greatly in the differential diagnosis.

In a third group of cases the flow of blood from the heart or great vessel may be so rapid as to prevent complete escape of blood into the pleural space or a clot may form in the opening in the pleura and prevent further

escape of blood from the pericardium. In this situation the symptoms will be that of extreme shock from massive blood loss coupled with a later appearance of tamponade.

SYMPTOMS OF CARDIAC TAMPONADE

The manifestations of tamponade are a weak, feeble pulse, decreased systolic blood pressure, increased venous pressure, narrow pulse pressure. In the acute rapidly developing type of tamponade the heart sounds are usually absent or diminished. X-rays are usually not very helpful in determining the presence of tamponade; however, as noted above, they may be extremely informative in showing a massive effusion of blood into the pleural space. The patient may exhibit a great deal of mental confusion and since many of the patients one sees have been stabbed in the course of alcoholic drinking bouts, the physician must be aware of the pitfall of attributing the confusion to the state of alcoholism.

TREATMENT OF STAB WOUNDS OF THE HEART

All penetrating and perforating wounds of the heart do not require thoracotomy and as a matter of fact there are some wounds that are probably best handled by conservative methods. Many patients with a stab wound of the heart can be managed very successfully by conservative methods. We prefer to utilize conservative therapy in the individual who does not exhibit signs or symptoms of massive blood loss and in whom the instrument that has created the damage is small in caliber. In this type of case aspiration of the pericardial sac with removal of relatively small amounts of blood usually corrects the symptoms referable to tamponade. We prefer to *aspirate the pericardium by introducing a* long #17 or #15 needle immediately beneath and to the left of the xiphoid process. The needle is directed cephalad at an angle of 45 degrees. It can be felt to penetrate the diaphragm and pericardium and at this point the aspiration usually can be carried out without difficulty. One can gently advance the needle until it can be felt to impinge on the pulsating heart. Aspiration through the xiphosternal angle is safer than aspiration anteriorly through the chest inasmuch as the coronary vessels will not be subject to injury. Furthermore, the blood tends to accumulate posteriorly and aspiration through this posterior angle of approach is *more successful*. Small stab wounds of the ventricle tend to seal rather promptly and in such cases frequently one or *at the most two aspirations of* the pericardial sac will usually suffice to correct signs of tamponade. Should the signs and symptoms of tamponade recur shortly requiring frequent aspirations, then conservative therapy should be abandoned and a thoracotomy with a pericardiotomy done with direct exposure and suture of the wound of *the heart*.

Conservative therapy should not be used or should be abandoned under certain conditions. *First, if aspiration does not relieve* tamponade, surgery must be instituted immediately. Secondly, when the tamponade recurs rapidly despite aspiration and finally when there is massive bleeding into the pleural cavity or if there is considerable external bleeding, surgical intervention should be attempted immediately.

DESCRIPTION OF SURGERY FOR WOUNDS OF THE HEART AND GREAT VESSELS

The best approach to wounds of the heart is a transpleural one usually *through the third* or fourth intercostal space. The incision is usually made through the left chest although

the right approach may be used when the wound of entrance indicates an injury to the portion of the heart protruding towards the right pleural space. One may readily divide the adjacent cartilages to provide good exposure and the surgeon should not hesitate *to divide the sternum transversely* and extend the incision into the opposite pleural space should this be necessary to provide adequate exposure. It is most important to obtain an adequate chest wall incision before opening the pericardial sac since occasionally very massive bleeding will occur from the atria or the intrapericardial vessels or even *from the ventricle when the pressure* on the wound is released or a clot is displaced by opening the pericardium. The surgeon must be in a position to place a finger over the *wound promptly after opening the pericardium*. Manipulation of the heart which some*times is poorly tolerated will be minimized by* first obtaining an adequate chest wall incision. *We do not* advise placing a *traction suture in* the apex of the heart for manipulation of the *heart as has been described in some of the* earlier text books. Bleeding from the ventricle can usually be readily controlled by finger pressure of the left hand while the surgeon places deep traction sutures beneath the finger. After the traction sutures have been placed and held in position a more accurate closure of the myocardium can be done by approximation sutures of 000 silk or 0000 silk on a fine curved needle. Care must be taken to avoid interference with the coronary circulation. A wound that passes parallel or very near a coronary vessel can be closed readily by passing a mattress type of suture completely beneath the coronary vessel so as to avoid interference with its lumen. Laceration of a coronary vein may be troublesome and require suture or ligature with fine arterial silk. Lacerations to major branches of the coronary artery may be sutured with fine arterial silk; however, it is probably better to attempt control of the bleeding from a coronary vessel by suturing a piece of muscle over the vessel or, if available, a thin piece of Ivalon sponge over the rent in the coronary vessel. Lacerations of the atria or great vessels should first be clamped with a non-crushing type of forceps and the laceration then closed with a running stitch in a dry field. A clamp can be placed tangentially to the vessels so as not to interfere with the flow of blood during this maneuver. An attempt to suture a major blood vessel with*out first placing a clamp tangentially* across the base of the laceration will usually result in tearing out of the sutures and increasing the difficulty in closing the laceration.

Traumatic aneurysm occasionally occurs following injury to the major vessels. This type of aneurysm is readily correctable and unless corrected the aneurysm will slowly enlarge and eventually perforate. For this reason the physician must be alert to this possibility and advise follow-up x-rays of the chest on all severe crushing injuries.

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Author Index

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F

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M